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# Ph.D.

# CHEMICAL SCIENCES

**XXX Cycle**

**Ph.D. Dissertation**

# Application of analytical methods for characterization of waste and recovered solvents

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**PREFACE**

The topic of this dissertation is the research of an analytical method for the determination of volatile organic compounds, in environmental matrix. This research was performed in a pharmaceutical manufacturing plant. This pharmaceutical plant uses a large amount of organic compounds for their manufacturing processes and the implementation of a program of waste management is a key aspect of this plant.

An example of waste management is the process of "Solvent Recovery" which is fundamental to recover organic solvents to be re-used and to control the environmental impact of the processes. The process of the Solvent Recovery following the first use in the manufacturing process has been the scope of the study.

This project is focalised on defining an analytical method for the determination of several types of volatile organic compounds and it is applied to control the processes of solvent recovery.

"Solvent Recovery" consists in the distillation and purification of organic solvents, with the objective to produce pure solvent or mix of solvents that are then re-used in the manufacturing industrial processes.

It is a strategy of this pharmaceutical industry for a sustainable environment and the solvent recovery represents a growing business in waste management. In fact, environmental protection is often an important prerogative of any new process and new industrial technologies.

Official analytical methods for analysis of solvents, in environmental matrix, specified the compounds and conditions to carry out an analysis. In this work, the method EPA 8015D is evaluated as preferential method for the analysis. This method is enhanced for a great number of solvents.

Purpose of this work has been the definition of rapid and reliable analytical method for the determination of solvents in the recovered solvents.

Organic solvents take part of the pharmaceutical processes as the medium of synthesis reaction end extraction.

The determination of a solvent, in an environmental matrix, has many analytical difficulties which are related with the high volatility and sampling technique for this kind of matrix.

**INTRODUCTION**

## 2. Compliance with the regulations requirements

Legislative Decree n° 3 April 2006, n° 152 promotes a high quality of human life through the management of environmental conditions and of natural sources. Any human organization must guarantee the protection of the environment and natural ecosystem through action of prevention of pollution and by evaluation of the environmental impact of production processes. The regulations promote sustainable development to ensure that the activities that satisfy all the needs of current generations do not compromise the quality of life of future generation.

The environmental assessment of plans, programs and projects became important to ensure that human activity is compatible with sustainable development: protection of human health, better quality of life, maintain the species and maintain of the capacity of reproduction of the ecosystem.

The installation of new manufacturing plants and or substantial modification of operations need the request for Integrated Environmental Authorization that contain information about: the installation, type and scope of the

installation, raw and auxiliary materials, substances and energy used by plant, the source of emissions of the plant. The control and the prevention of emission is important for a sustainable activity.

The regulation confirms the importance of the waste management: the objective is the reduction of waste deposal through action of valorisation of the waste. The waste is not only something that is became useless, but also it could have a second life: the waste became starting material for the production of secondary raw material[1].

The Directive 2008/1/EC on Integrated Pollution Prevention and Control (IPPC Directive) achieves integrated prevention to control pollution and it lays about the adoption of specific measure to reduce emissions level in the air, in the water and in the land. The general principles of this directive are based on the safety for the environment: all member states shall take the necessary measures to provide that all the installations operate in accordance with the following requirements:

- use of the best technical solution to prevent pollution
- avoid waste production, and recovery action for wastes and reducing of emissions and environmental impact when wastes are produced
- efficient use of energy
- take necessary measures to prevent accidents and limit their consequences.

In the Annex III of the Directive 2008/1/EC there is a list of substances that can affect the safety of the environment:

- Quality of the air: sulphur dioxide and other sulphur compounds; oxides of nitrogen and other nitrogen compounds; carbon monoxide; volatile organic compounds (VOC), metals and other compounds, dust, asbestos (suspended particulates, fibres); chlorine and its compounds, fluorine and its compounds, arsenic and its compounds, cyanides; substances and preparation which have proved to have carcinogenic or mutagenic properties or properties which may affect reproduction via the air
- Quality of the water: organohalogen compounds and substances which may form such compounds in the aquatic environment; organophosphorous compounds; organotin compounds, substances and preparation which have proved to have carcinogenic or mutagenic properties or properties which may affect reproduction via the aquatic environment, persistent hydrocarbons and persistent and bioaccumulable organic toxic substances; cyanides; metals and their compounds; arsenic and its compounds; biocides and plant health products, materials in suspension, substances which contribute to eutrophication (in particular nitrates and phosphate); substances which have an unfavourable influence on the oxygen balance (and can be measured using parameters such as BOD, COD, etc)[2]

To persecute the scope of the safety of human health and of the environment is necessary a correct use of chemical substances in all the steps of the process. The Classification, Labelling and Packaging (CLP) Regulation (EC No 1272/2008) ensures a high level of protection of health and environment and it describes the rules for classification and labelling of substances and mixtures. CLP requires manufacturers, importers or downstream users of substances or mixtures to classify label and package their hazardous chemicals appropriately before placing them on the market and use for many kinds of applications. CLP is very

[1]DecretoLegislativo 3 aprile 2006, n. 152
[2]Directive 2008/1/EC on Integrated Pollution Prevention and Control (IPPC Directive)

determinant to communicate the hazardous of a substance or a mixture. When relevant information, such as toxicological data, are available for a substance or a mixture, the CLP assigns a certain hazard class and category. After the classification, the hazards of a substance or a mixture must be communicated to other actors of supply chain[3].

| CLP Regulation No 1272/2008 | Example of hazard statement | Example of precautionary statement |
|---|---|---|
|  | Heating may cause an explosion | Keep away from heat/sparks/open flames/hot surfaces. – no smoking |
|  | Heating may cause a fire | Keep only in original container |
|  | May intensify fire; oxidizer | Take any precaution to avoid mixing with combustibles |
|  | Causes serious eye damage | Wear eye protection |
|  | Toxic if swallowed | Do not eat, drink or smoke when using this product |
|  | Toxic to the aquatic life with long lasting effects | Avoid release to the environment |
|  | May cause allergy or asthma symptoms or breathing difficulties if inhaled | In case of inadequate ventilation wear respiratory protection |
|  | May cause an allergic skin reaction | Contaminated work clothing should not be allowed out of the workplace |
|  | Contains gas under pressure; may explode when heated | Protect from sunlight. Store in a well ventilated place |

Figure 1: Pictograms for hazardous substances according with Classification, Labelling and Packaging (CLP)

**2. Life Cycle Assessment (LCA)**

Nowadays we live in the world affected by energy crisis, because of the dependence of many human activities by non-renewable energy source and their inefficient use. Biofuels have received a great attention in order to reduce the dependence on fossil fuels[4]. Studies of "Life Cycle Assessment (LCA)" demonstrate a positive approach of the reconversion of wastes in useful materials and substances[5].

The LCA is an important tool of making decision to explore technical solutions to reduce the use of fossil fuels and to generate a low impact on environment.

[3]Regulation (EC) No 1272/2008 of the parliament and of the council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006, Official Journal of the European Union L 353/1

[4]PooyaAzadi, Robert Malina,Steven R.H. Barrett, Markus Kraft, The evolution of the biofuel science, *Renewable and Sustainable Energy Reviews 76 (2017) 1479–1484*

[5] Augustine Quek , RajasekharBalasubramanian, Life Cycle Assessment of Energy and Energy Carriers from Waste Matter e A Review, *Journal of Cleaner Production 79 (2014) 18 - 31*

Sustainable Development of productive processes imply an approach of LCA of all steps of industrial production. Modern chemical industries evaluate how their activities affect the environment and nowadays the choice of "greener" processes and products is a key aspect to minimise environmental impact[6].

"Life Cycle Assessment" is an approach to assess industrial system that begin with the evaluation of raw material originated from the earth and it ends when all materials come back to earth. LCA evaluates all stages of product's life, which are interdependent, so this approach enables the estimation of cumulative environmental impact that came from all stages of the production.

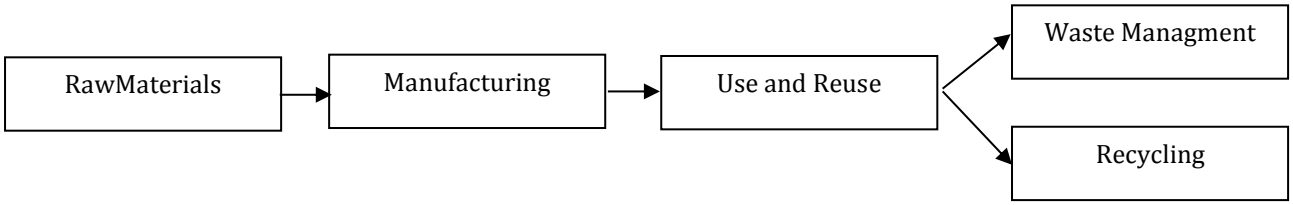


Figure 2: Steps of Life Cycle Assessment.

LCA helps to manage environmental impact underlying the importance of a correct planning of different material used in the processes: for example use and reuse of substances.

The LCA methodology includes the following steps (ISO 14040 2006):

- Goal definition: the study of the process
- Inventory analysis: identification and quantification of all energies and materials used and of all environmental emissions
- Impact assessment: involves the evaluation of human and ecological effects from the inventory.
- Interpretation: the evaluation of the data to make a decision on which process or product is environmental friendly and sustainable

LCA is applied by many kinds of industry: pharmaceutical, electronic, fuel manufacturer, ecc…[7]

Pharmaceutical industry uses a large quantity of solvent for the synthesis of active principles and, after their use, incineration of waste solvents is a common practice. The implementation of solvent recovery plant allows the minimization of emissions and the reduction of solvents deposal. Organic solvents are used as reaction medium for the synthesis of many complex molecules called "Active Pharmaceutical Ingredient (API)". Solvents represent a very big portion of wastes produced by pharmaceutical industry: they are used for synthesis, purification and washing operation of API[8].

[6]Adeel Tariq, Yuosre F. Badi, Waqas Tariq, Umair Saeed Bhutta, Drivers and consequences of green product and process innovation:A systematic review, conceptual framework, and future outlook, *Technology in Society 51 (2017) 8-23*

[7]M.A.Curran,Life Cycle Assessment: Principles and Practices, United States Environmental Protection Agency, National Risk Management Research Laboratory, Cincinnati, Ohio, 2006

[8] Michael J. Raymond, C. Stewart Slater and Mariano J. Savelski, LCA approach to the analysis of solvent waste issues in the pharmaceutical Industry, *GreenChem., 2010,12, 1826–1834*

**3. Analytical Procedures for quality control in pharmaceutical industry**

Organic solvents are necessary for production processes of pharmaceutical products, but it is necessary to remove all solvents from the final products at the end of the process.

Analytical procedures used during quality control analysis of pharmaceutical products are based on the use of gas chromatography to separate all the components. The identification is made by Flame Ionization Detector (FID) or by Mass Spectrometry (MS). Many analytical methods are specific for a limited number of solvents and sample matrices.

It is necessary to study the analytical procedures for a large number of solvents and their residual determination. The solvents are necessary during the production processes as reaction medium and for purification operations, such as crystallization. The determination of residual solvents in pharmaceutical products is necessary, because of their toxicity and their hazardous for human health and the environmental impact. The solvents can also induce transformation of active substances, potentially losing their biological activity and causing the decomposition of the products.

Another important aspect is a forensic interest in the determination of contaminants of pharmaceutical products: the profile of contaminants could be used as a fingerprinting of manufacturer to avoid counterfeit of pharmaceuticals [9].

A classification of solvents based on their toxicity is possible as follows[10]:

- *Class I solvents*: the use of these solvents should be avoided because they are carcinogens and very dangerous for the environment
- *Class II solvents*: the use of these solvents should be limited because they are non-genotoxic animal carcinogens, but they cause other irreversible toxicity such as neurotoxicity or teratogenicity.
- *Class III solvents*: they are solvents with low toxicity for human health.

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[9]Analytical procedures for quality control of pharmaceuticals in terms of residual solvents content: Challenges and recent developments, MaciejTankiewicz, , Jacek Namies´nik, WiesławSawick, *Trends in Analytical chemistry 80 (2016) 328–344*

[10]lCH guideline Q3C (R6) on impurities: guideline for residual solvents EMA/CHMP/ICH/82260/2006

The most used solvents in pharmaceutical industry are summarized in the following Table 1:

| **Class of Solvents** | **Compounds** |
|---|---|
| Alcohols | Methanol, ethanol, propanol, isopropanol, butanol, isobutanol, propylene glycol |
| Aliphatyc Hydrocarbons | Hexane, cyclohexane, isooctane |
| Amides | Dimethylformamide |
| Amines | Pyridyne |
| Aromatic hydrocarbons | Toluene, xylenes |
| Esters | Ethyl acetate, butyl acetate |
| Ethers | Ethyl ether, 1,4-dioxane, tetrahydrofuran, tert-butyl methyl ether, diisopropyl ether |
| Alogenated Solvents | Dichloromethane, chloroform, carbon tetrachloride, trichloroethane, ethylene bromide, tetrachloroethylene |
| Ketones | Acetone, methyl ethyl ketone, methyl isobutyl ketone, methyl isopropyl ketone |
| Nitriles | Acetonitrile |
| Sulfur containing | Dimethyl sulfoxide |
| Water | - |

Table 1: The most used solvents in Pharmaceutical Industry

**4. Solvent Recovery**

The solvents are produced from petrochemicals feedstocks or by chemical processes and they are largely used in chemical plants. After their use the solvents are recycled or sent to disposal.

A typical operation of disposal of solvents is incineration: the combustion of waste solvents produces a large amount of exhaust gases and wastewater and it is necessary to treat wastewater to reduce their environmental impact.

The recovery of waste solvents is very important in the pharmaceutical, chemical and petrochemical industries. A large amount of production costs of pharmaceutical industry are imputed to downstream processing in which numerous solvents and mix of them are used to purification operations.

It is interesting for industry to find technical solutions that allow recovering solvents to be reused for their needs[11].

[11] Eduardo J., Cavanagh, Mariano J.Savelski, C.Stewart Slater, Optimization of environmental impact reduction and economic feasibility of *solventwasterecovery* using a new software tool, *Chemical Engineering Research and Design, 9 2 ( 2 0 1 4 ) 1942–1954*

The presence of organic solvents in wastewater evidences an inefficient use of resources and this is a problem because of the hazardous for the human health and the environment.

In accordance with the general principle of Directive 2008/1/EC on Integrated Pollution Prevention and Control (IPPC Directive), chemical industries must adopt preventive measures and the best available techniques to recover and recycle wastes. The waste prevention means the adequacy of measures for the correct use of chemical substances before they became wastes and their re-use or recovery. Recycling indicates a procedure focused on reprocessing a material for the same or different kind of industrial process. Recovery indicates a technical procedure for the regeneration of a material with the same characteristics.

Chemical industries that use a large amount of solvents, such as pharmaceutical industry, have to adopt measures for the control of the presence of solvents in wastewater with analytical procedures. The development of analytical procedures is strategical to verify the adopted measures of prevention and the compliance with regulations requirements. In chemical plants, the recovery of solvents, with added value, is preferred compared to the disposal. The implementation of technical solution for recovering is the best strategy for industries that uses a large amount of solvents because of economic benefit that derives from recovery and the minimization of dangerous wastes and the emissions in the environment. The recovery of solvents from water and the wastewater depuration is the best solution to reduce environmental impact of industrial activities.

Solvent Recovery process is a technical challenge because of the difficulties of recovering high amounts of pure solvents and mix of solvents: it depends by the starting matrices that are different in solvent and water content; then many solvents generate azeotropes with difficulties in the separation by distillation.

A particular solution to separate solvents from aqueous matrix (Abejon R et al.) is the use of organic solvents resistant nanofiltration membranes. The separation of solutes by nanofiltration is based on the difference between their molecular weights and their molecular sizes: a good separation is obtained when there is a high difference in terms of molecular weights and sizes. The separation is very difficult when there is a very low difference; in this case, the separation by nanofiltration needs many steps[12].

Another example of innovative system to remove organic solvent is the operation with membranes (V. Garcia et al.) A quaternary system with water, sodium chloride, dichloromethane and n-butanol is processed by pervaporation and operation with hydrophobic membranes: the first membrane is made of polysiloxanepolymer with an active layer thickness of 0.01 mm, the second membrane is a dense membrane of 0.125 mm made of dimethyl and methyl vinyl siloxane copolymers[13].

**5. Analytical Methods for determination of VOC**

Analytical testing requests for a sample of waste recovered solvents are usually: pH, density, water content (% w/w) and the concentrations of the different compounds.

These analyses are crucial to control the Solvent Recovery process to transform the waste solvent in a secondary raw material.

[12]Abejon R., Garea A., Irabien A., 2015, Organic solvent recovery and reuse in pharmaceutical purification processes by nanofiltration membrane cascades, *Chemical Engineering Transactions, 43, 1057-1062 DOI: 10.3303/CET1543177*

[13]VerónicaGarcía, Eva Pongrácz, Paul S. Phillips, Riitta L. Keiski,From waste treatment to resource efficiency in the chemical industry: recovery of organic solvents from waters containing electrolytes by pervaporation, *Journal of Cleaner Production 39 (2013) 146e153*

Water content influences the prices of recovered solvents: samples with a high water percentage are less interesting in this business, while samples with a high solvents content are more interesting. The knowledge of the composition of the samples of waste solvents plays a pivotal role for the right decision-making, based on the performance of industrial process of solvent recovery.

Distillation is an operation able to separate different compounds based on the different volatility using a series of distillation columns with a particular set of temperature to perform the best and efficient separation. The presence of an azeotropic mixture contributes to make difficult the entire process. Industries have the need to control all the process through efficient analytical methods able to give a rapid response.

The development of gas chromatography is a determining factor for analysis of volatile organic compounds (VOC). The research and development of analytical methods to determinate the concentration of VOC in different environmental matrices have nowadays a growing interest because of the impact of these compounds to various environmental systems. Many effects of VOC are recognized: stratospheric ozone depletion, tropospheric photochemical ozone formation, toxic and carcinogenic human health effects, aggravate the global greenhouse effect and accumulation as pollutants in the environment.

Instrumental analysis is based on the use of gas chromatography coupled with different types of detectors: Flame Ionization Detector (FID); Electron Capture Detector (ECD), Photoionization Detector (PID) and Mass Spectrometry (MS).

There is a huge amount of interesting work for the determination of VOC in environmental matrices[14] [15] [16] [17].

It's very interesting to know analytical methods able to detect a huge amount of compounds.

The determination of VOC in surface water and wastewater is carried out by Purge and Trap–Gas Chromatography–Mass Spectrometry method[18]. The investigation of VOC in surface water and wastewater is important to evaluate the pollution and give the opportunity to make correlation between human activities and environmental impact. The development of efficient analytical method could help to control environmental impact.

Analytical methods for determination of VOC take into account the range of concentration of interest. Dynamic headspace chromatography is based on the maximization of the contact between gas and the surface or the internal of the sample allowing the concentration of the compounds in the trap. Analytical methods based on the

[14]Ruth Barro, Jorge Regueiro, MaríaLlompart, Carmen Garcia-Jares, Analysis of industrial contaminants in indoor air: Part 1. Volatile organic compounds, carbonyl compounds, polycyclic aromatic hydrocarbons and polychlorinated biphenyls, *Journal of Chromatography A, 1216 (2009) 540–566*

[15]Jo Dewulf, Herman Van Langenhove, Anthropogenic volatile organic compounds in ambient air and natural waters: a review on recent developments of analytical methodology, performance and interpretation of field measurements, *Journal of Chromatography A, 843 (1999) 163–177*

[16]Kristof Demeestere, Jo Dewulf, Bavo De Witte, Herman Van Langenhove, Sample preparation for the analysis of volatile organic compounds in air andwater matrices, *Journal of Chromatography A, 1153 (2007) 130–144*

[17]Martin Harper, Sorbent trapping of volatile organic compounds from air, *Journal of Chromatography A, 885 (2000) 129–151*

[18]Anastasia D. Nikolaou, Spyros K. Golfinopoulos, Maria N. Kostopoulou, George A. Kolokythas, Themistokles D. Lekkas, Determination of volatile organic compounds in surfacewaters and treated wastewater in Greece, *Water Research 36 (2002) 2883–2890*

use of Dynamic headspace chromatography offers the advantage of determination of very low concentration of VOC and they revealed successful to detect residual solvent in pharmaceutical preparation[19].

**6. Factors that can affect the analysis**

A particular attention is regarded to the sampling methodologies based on the use of different sampling systems specific for different compounds: the research about adsorbent materials has nowadays a growing interest.

Analytical quality assurance for the analysis of VOC in environmental matrices is an important aspect: the compounds of interest are affected by several factors that could compromise the analysis: sampling methodology, transport conditions, maintenance, extraction and instrumental conditions.

For example, air sampling systems for VOC detection are manufactured with different sorbent matrices, such as: activated carbon, silica gel, polydimethylsiloxane.

The problem with air sampling is the absorption of water, which can affect the sampling; it is important to use material with a high specificity for the molecules of interest and able to avoid the absorption of the water.

The sampling of water for the determination of VOC is affected by different factors: transport and maintenance condition and the subsequent analysis is influenced by extraction methodologies.

The liquid-liquid extraction is ideal to extract VOC from water by organic solvent, but the disadvantage is in the correct choose of the solvent, different from analytes, and in recovery efficiency.

The development of dynamic headspace technique is ideal for VOC extraction from water samples: the extraction of compounds of interest is performed by purge and trap system. Bubbling a gas stream in the water samples, the inert gas enriches with volatile compounds, and then the enriched gas led through a sorbent matrix in which volatile compounds are retained. Subsequently the VOC are desorbed from sorbent matrix and they are injected in GC column. The major advantage of purge and trap is that a high percentage of VOC are successfully injected with a better analytical response.

To evaluate analytical performance of an analytical method, it is important to take in consideration some criteria associated with the quality of analytical data: Limit of detection, Limit of quantification, Reproducibility, Repeatability, Accuracy, Calibration curve, Specificity, Range of application[20].

Waste solvents samples are very complex matrices: they are heterogeneous solutions with solid and liquid phase.

Complex samples could be characterized by a biphasic liquid system with a solid residual. In these particular cases, the sampling is very problematic because of the difficulties to generate a representative sample from container with a content of thousands of litres of waste solvent.

The testing laboratory needs to complete the analysis in order to characterize the effective composition of the samples, but a waste solvent contains solid residuals, water, pharmaceutical waste, solvents mixture in one or two phases.

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[19]Claudia Witschi, Erik Doelker, Residual solvent in pharmaceutical products: acceptable limits, influences on physicochemical properties, analytical methods and documented values, European Journal of Pharamceutics and Biopharmaceutics 43 (1997) 215-242

[20]Jo Dewulf, Herman Van Langenhove, Anthropogenic volatile organic compounds in ambient air andnatural waters: a review on recent developments of analytical methodology, performance and interpretation of field measurements, *Journal of Chromatography A, 843 (1999) 163–177*

The attention is concentrated on the determination of VOC content in the samples based on a specific request of the customers who are interested to agree regulations and to recover the maximum amount of solvents.
The difficulties associated with the analytical approach with this kind of samples are in the pre-treatment of the samples. For example, for a complex sample, that shows biphasic liquid system and solid, a sequence of steps is necessary: it is possible to quantify the solid by evaporation of solvent and to analyse separately the phases in the samples. In this case, the step of pre-treatment is a critical aspect for the expression of the correct analytical results.

**7. Method EPA 8015D**

The samples of waste solvents can be analysed with official method EPA 8015D. This method may be used to determine the concentration of volatile organic compounds (VOC) and semi-volatile organic compounds by gas chromatography. The following list shows the compounds that can be analysed by official method EPA 8015D:

- Acetone
- Acetonitrile
- Acrolein
- Acrylonitrile
- Allyl alcohol
- t-Amyl alcohol (TAA)
- t-Amyl ethyl ether (TAEE)
- t-Amyl methyl ether (TAME)
- Benzene
- t-Butyl alcohol (TBA)
- Crotonaldehyde
- Diethyl ether
- Diisopropyl ether (DIPE)
- Ethanol
- Ethyl acetate
- Ethyl Benzene
- Ethylene oxide
- Ethyl *tert*-butyl ether (ETBE)
- Isopropyl alcohol (2-Propanol)
- Methanol
- Methyl ethyl ketone (MEK, 2-Butanone)
- Methyl *tert*-butyl ether (MTBE)
- *N*-Nitroso-di-*n*-butylamine
- Paraldehyde
- 2-Pentanone
- 2-Picoline
- 1-Propanol (*n*-Propylalcohol)

- Propionitrile
- Pyridine
- Toluene
- *o*-Toluidine
- *o*-Xylene ,
- *m*-Xylene,
- *p*-Xylene

This method is also for the quantitation of trietilammine and it finds application for the characterization of petroleum samples. The method allows the analysts to add other analytes, but it is important to demonstrate the performance of analytical method.

The flame ionization detector is a non-selective detector and it is necessary to consider the presence of interfering compounds. Samples with a large amount of different compounds can show problems of resolution. The confirmation of the different molecules is necessary and a GC-MS could be used to make a qualitative analysis.

Quality control procedure are necessary to demonstrate the best performance of the systems of analytical laboratory. The first control is the blank to demonstrate the absence of interfering compounds and to control instrumental signal of the blank; the control of calibration is necessary to validate the calibration curve and quantitative analysis; the matrix spike samples are necessary to control the recovery of the method[21].

**8. Method EPA 8260C**

The Method EPA 8260C allows the determination of VOC by GC-MS for different kinds of environmental matrices. In the list below the principal compound of interest for this method[22]:

- Acetone
- Acetonitrile
- Acrolein (Propenal)
- Acrylonitrile
- Allyl alcohol
- Allyl chloride
- t-Amyl ethyl ether (TAEE)
- t-Amyl methyl ether (TAME)
- Benzene
- Benzyl chloride
- Bis(2-chloroethyl)sulfide
- Bromoacetone
- Bromochloromethane
- Bromodichloromethane

[21]Method EPA 8015D, Non-halogenatedorganicsusing GC-FID, *Revision 4 June 2003*
[22]Method 8260C, Volatile Organic Compunds by gas chromatography / Mass Spectrometry

- 4-Bromofluorobenzene (surr)
- Bromoform
- Bromomethane
- n-Butanol
- 2-Butanone (MEK)
- t-Butyl alcohol
- Carbon disulfide
- Carbon tetrachloride
- Chloral hydrate
- Chlorobenzene
- Chlorobenzene-d5 (IS)
- Chlorodibromomethane
- Chloroethane
- 2-Chloroethanol
- 2-Chloroethyl vinyl ether
- Chloroform
- Chloromethane
- Chloroprene
- Crotonaldehyde
- 1,2-Dibromo-3-chloropropane
- 1,2-Dibromoethane
- Dibromomethane
- 1,2-Dichlorobenzene
- 1,3-Dichlorobenzene
- 1,4-Dichlorobenzene
- 1,4-Dichlorobenzene-d4 (IS)
- cis-1,4-Dichloro-2-butene
- trans-1,4-Dichloro-2-butene
- Dichlorodifluoromethane
- 1,1-Dichloroethane
- 1,2-Dichloroethane
- 1,2-Dichloroethane-d4 (surr)
- 1,1-Dichloroethene
- trans-1,2-Dichloroethene
- 1,2-Dichloropropane
- 1,3-Dichloro-2-propanol
- cis-1,3-Dichloropropene
- trans-1,3-Dichloropropene
- 1,2,3,4-Diepoxybutane
- Diethyl ether

- Diisopropyl ether (DIPE)
- 1,4-Difluorobenzene (IS)
- 1,4-Dioxane
- Epichlorohydrin
- Ethanol
- Ethyl acetate
- Ethylbenzene
- Ethylene oxide
- Ethylmethacrylate
- Fluorobenzene (IS)
- Ethyl tert-butyl ether (ETBE)
- Hexachlorobutadiene
- Hexachloroethane
- 2-Hexanone
- Iodomethane
- Isobutyl alcohol
- Isopropylbenzene
- Malononitrile
- Methacrylonitrile
- Methanol
- Methylene chloride
- Methyl methacrylate
- 4-Methyl-2-pentanone (MIBK)
- Methyl tert-butyl ether (MTBE)
- Naphthalene
- Nitrobenzene
- 2-Nitropropane
- N-Nitroso-di-n-butylamine
- Paraldehyde
- Pentachloroethane
- 2-Pentanone
- 2-Picoline
- 1-Propanol
- 2-Propanol
- Propargyl alcohol
- β-Propiolactone
- Propionitrile (ethyl cyanide)
- n-Propylamine
- Pyridine
- Styrene

- 1,1,1,2-Tetrachloroethane
- 1,1,2,2-Tetrachloroethane
- Tetrachloroethene
- Toluene
- Toluene-d8 (surr)
- o-Toluidine
- 1,2,4-Trichlorobenzene
- 1,1,1-Trichloroethane
- 1,1,2-Trichloroethane
- Trichloroethene
- Trichlorofluoromethane
- 1,2,3-Trichloropropane
- Vinyl acetate
- Vinyl chloride
- o-Xylene
- m-Xylene
- p-Xylene

The application of GC-MS has the advantage of a higher instrumental sensibility allowing the simultaneous identification and quantification.

**9. Scope of the work**

Objective of this work was the development of an analytical method, in accordance with official method EPA 8015D, for the determination of Volatile Organic Compounds (VOC) in waste solvents and secondary raw materials. This analytical method is focused for the determination of high concentration of solvents.

This project was carried out inside a pharmaceutical plant in which a distillation plant is implemented for the recovery of waste solvents and their transformation in secondary raw materials: this is the goal of "Solvent Recovery".

This work shows the presentation and the statistical elaboration of results obtained following the iter of validation of the analytical method. The interest was focused on recovery data to evaluate the precision, accuracy and reproducibility of the analytical method.

The evaluation of *z-score*, recovery and the Analysis of Variance (ANOVA) played a pivotal role to demonstrate the validity of the purpose of this work.

The analytical method developed was focused for the determination of the following compounds:

- Methanol
- Ethanol
- Isopropanol
- Acetone
- Acetonitrile
- Methyl Acetate

- Dichloromethane
- Hexane
- 2-Butanone
- Ethyl Acetate
- Tetrahydrofuran
- Cyclohexane
- Isopropyl Acetate
- Heptane
- 1,4-Dioxane
- Cyclopentyl Methyl Ether
- Toluene
- Butyl Acetate
- N,N-Dimethylformamide
- 2-Butanol
- 1-Butanol
- Pyridine
- Diisopropyl ether
- Octane

These compounds were the most frequently requested by the customers because their diffusion in pharmaceutical processes. Their hazard for environment and for human health is known, so their recover and re-use is pivotal to reduce their impact.

The importance of this work derives from the needs to implement an analytical method able to investigate different compounds assuring an high quality of analytical data.

**MATERIALS AND METHODS**

### 1. Analytical reagents and suppliers

Methanol; Ethanol; Isopropanol; Acetone; Acetonitrile; Methyl acetate; Dichloromethane; Hexane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide; 2-Butanol; 1-Butanol; Pyridine; Diisopropylether; Octane are acquired from Sigma Aldrich. Pentane was purchased from Scharlab.

Certified matrix with a composition of Methanol, Ethanol, Isopropanol, Acetonitrile, Ethyl Acetate, Toluene was purchased from Restek.

Methanol with 0,0005% of water content purchased from Scharlab and Titrant for Karl Fischer without pyridine was used for determination of water by Karl Fischer's titrimetric method was purchased from Merck (Sigma Aldrich).

### 2. Instruments

A GC-FID-NPD 7820 A of Agilent with software Open Lab CDS Rev.C.01,07 was used for separation and quantification of analytes.This Instrument was called in this work "GC-FID_Principal".

The instrumental operative conditions are described as follow:

- GC Oven Temperature Setpoint On
- Initial Temperature 40 °C
- Hold Time 20 min
- Post Run 50 °C
- Program: Rate 15 °C/min; Final Temperature 250 °C; Hold Time 10 min
- Equilibration Time 1 min
- Max Temperature 300 °C
- Syringe Size 10 µL
- Injection Volume 1 µL
- Mode Split
- Heater On 300 °C
- Pressure On 7.3001 psi
- Gas Saver On 20 After 3 min mL/min
- Split Ratio 20 :1
- Split Flow 110 mL/min
- Column: Mega 15191 Vocol Fused Silica; diameter 530.00 µm; length 60.0 m; film thickness 3.00 µm; maximum temperature 300.0 °C; Flow 5.5 ml/min
- Make up gas: Helium
- Make up flow: 30.0 ml/min
- Hydrogen flow: 45.0 ml/min
- Air Flow: 400.0 ml/min

A GC-FID of Shimadzu with software GC Solution was used for separation and quantification of analytes. This Instrument was called in this work "GC-FID_Control".

The instrumental operative conditions are described as follow:

- GC Oven Temperature Setpoint On
- Initial Temperature 40 °C
- Hold Time 20 min
- Post Run 50 °C
- Program: Rate 15 °C/min; Final Temperature 250 °C; Hold Time 10 min
- Equilibration Time 1 min
- Max Temperature 300 °C
- Syringe Size 10 µL
- Injection Volume 1 µL
- Mode Split
- Heater On 300 °C
- Pressure On 7.3001 psi
- Gas Saver On 20 After 3 min mL/min
- Split Ratio 20 :1
- Split Flow 110 mL/min
- Column: Vocol+ BPX; length 85.0 m; diameter 530 µm; maximum temperature 300.0 °C; Flow 3.0 ml/min
- Make up gas: Helium
- Make up flow: 30.0 ml/min
- Hydrogen flow: 45.0 ml/min
- Air Flow: 400.0 ml/min

A GC-MS 5977 with headspace injector of Agilent with software Mass Hunter GC/MS Acquisition B.07.00.SP2.1654 equipped with a NIST library database was used for the identification of analytes in samples of solvent recovery.

The instrumental operative conditions are described as follow:

- GC Oven Temperature Setpoint On
- Initial Temperature 60 °C
- Hold Time 10 min
- Post Run 50 °C
- Program: Rate 10 °C/min; Final Temperature 120 °C; Hold Time 0 min; Rate 15 °C/min; Final Temperature 250 °C; Hold Time 3 min
- Equilibration Time 3 min
- Max Temperature 250 °C
- Mode Split
- Heater On 250 °C
- Pressure On 10.802 psi
- Gas Saver Off
- Split Ratio 10:1

- Split Flow 14.301 mL/min
- MSD Transfer Line, Temperature 230°C
- Column 1: Supelco 28662-U 52964-01B; diameter 180.00 µm; film thickness 1.00 µm; length 20.0 m; maximum temperature 300.0 °C; Flow 0.4806 ml/min
- Column 2: Agilent 122-1364; diameter 250 µm; film thickness 1.40 µm; length 60.0 m; maximum temperature 260.0 °C; Flow 1.4301 ml/min

A GC-MS 5977 with direct injection of Agilent with software Mass Hunter GC/MS Acquisition B.07.00.SP2.1654 equipped with a NIST library database was used for the identification of analytes in samples of solvent recovery. The instrumental operative conditions are described as follow:

- GC Oven Temperature Setpoint On
- Initial Temperature 40 °C
- Hold Time 12 min
- Post Run 70 °C
- Program: Rate 15 °C/min; Final Temperature 150 °C; Hold Time 0 min; Rate 20 °C/min; Final Temperature 260 °C; Hold Time 6 min
- Equilibration Time 0.25 min
- Max Temperature 260 °C
- Syringe Size 10 µL
- Injection Volume 1 µL
- Mode Split
- Heater On 110 °C
- Pressure On 23.708 psi
- Gas Saver On 20 After 3 min mL/min
- Split Ratio 15 :1
- Split Flow 22.5 mL/min
- MSD Transfer Line, Temperature 235°C
- Column: Agilent 122-1364; diameter 250 µm; film thickness 1.40 µm; length 60.0 m; maximum temperature 260.0 °C; Flow 1.5 ml/min

A Karl Fischer of Mettler Toledo was used for determination of water content in the samples.

## 3. Operative Procedures for analysis of samples of "Solvent Recovery"

### 3.1. Stock Solutions and Calibration Standards for GC-FID

Stock solutions for GC-FID called respectively "*Multi-standard SR1*", "*Multi-standard SR2*", and "*Multi-standard SR3*" were prepared from acquired pure standard materials weighting 1 ml of each solvent in a final volume of 25 mL of pentane. The composition of the three calibration standards are:

- *Multi-standard SR1*: Methanol; Ethanol; Acetone; Acetonitrile; Hexane; Isopropanol; Methyl acetate; Dichloromethane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide.
- *Multi-standard SR2*: 2-Butanol; 1-Butanol; Pyridine.
- *Multi-standard SR3*: Diisopropylether; Octane.

The stock solutions had a concentration of about 30000 mg/L for each solvent. Five calibration standards were prepared from stock solutions diluting with pentane to obtain a calibration curve in a concentration range between 1000 and 30000 mg/L. For this study, dilutions for calibration curve were about 1500; 6000; 15000; 22500; 30000 mg/L.
The Appendix, section A1 shows an example of calibration curve for all the compounds.

### 3.2. Analysis of the samples

All the calibrations were daily controlled with known concentration standards.
Periodically a quality control check with a certified matrix was evaluated to assure the quality of analytical data.
The samples of solvents (wastes, secondary raw materials) was characterized in term of water content (% w/w) through Karl Fischer's titrimetric method. A weighted small quantity of the sample was put inside the instrument for Karl Fischer titration through a syringe and the analysis is made automatically. The knowledge of water content is important because of the necessity of its elimination from the secondary raw material. The determination of mean water equivalence factor of Karl Fischer was carried out after 4 injection of weighted amount of water 100 % w/w and the mean value was taken in consideration for analysis. The performance of Karl Fischer method was daily verified with certified matrix with a water content of 1 % w/w.
VOC composition is determined through GC-MS with headspace injection or direct injection for qualitative analysis and GC-FID for quantitative analysis. The sample is directly injected in GC-FID without pretreatment.

## 4. Validation of the analytical method

### 4.1. Limit of Detection (LOD) and Limit of Quantification (LOQ)

The procedure for the determination of Limit of Detection (LOD) and Limit of Quantification (LOQ) implied the injection of 10 standard samples with a concentration range of 200-500 mg/L of all compounds of interest.
A stock solution, called "*Model Standard SR1*" was prepared weighting 1 ml of each compounds and diluting with acetone in a final volume of 25 mL.

- *Model Standard SR1*: Methanol; Ethanol; Acetonitrile; Hexane; Isopropanol; Methyl acetate; Dichloromethane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide.

The "Model Standard SR1" was diluted with acetone with a dilution factor of 20 to obtain the "Primary Dilution Solution" from which a calibration curve was obtained in a concentration range between 300-1500 mg/L for all compounds. The preparation of the "Model Standard SR1" allowed to study a model solution very similar with real samples of distillates of secondary raw materials and final products for the "Solvent Recovery".

**4.2. Experiments of repeatability on Certified Matrix**

Experiments of repeatability on Certified Matrix were performed on three levels of concentration (2000, 10000, 15000 mg/L) of methanol, ethanol, isopropanol, acetonitrile, ethyl acetate, toluene; each sample was prepared from certified matrix which were acquired for this specific purpose.

Starting from the "Certified Matrix", the preparation of three level of concentration by dilution in acetone, and the injection of seven samples for each level of concentration allowed the determination of the method's performance.

- *Certified Matrix*: Methanol, Ethanol, Isopropanol, Acetonitrile, Ethyl Acetate, Toluene

Each level of the concentration was injected in seven different vials and they were analyzed by GC-FID.

**5. Experiments of Recovery**

Experiments of recovery were carried out by the preparation of the Initial Calibration Verification (ICV) with a concentration closer at the centrum of the calibration curve (≈15000 mg/L).

Experiments to evaluate matrix effects take in consideration a Laboratory Control Standard (LCS) and a real matrix spiked with a known concentration of the same magnitude order of the LCS.

**6. Qualitative analysis by GC-MS**

A diluted sample with a dilution factor of 1000 in water was analyzed by GC-MS with headspace injection to identify all the components. In alternative, a diluted sample with a diluition factor in methanol was analyzed by GC-MS with direct injection to identify all the components. After the identification, all the samples are quantified by GC-FID.

**7. Quantitative analysis by GC-MS with direct injection**

Stock solutions called respectively "*Multi-standard MS-SR1*", "*Multi-standard MS-SR2"* were prepared from acquired pure standard materials weighting 100 μl of each solvent and diluted in methanol in a final volume of 25 mL:

- *Multi-standard MS-SR1*: Ethanol; Acetone; Acetonitrile; Hexane; Isopropanol; Methyl acetate; Dichloromethane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide.
- *Multi-standard MS-SR2*: Diisopropyleter; 2-Butanol; 1-Butanol; Pyridine; Octane.

The stock solutions had a concentration of about 3000 mg/L for each solvent. Five calibration standards are prepared from stock solutions diluting with methanol (dilution factor 10) to obtain a calibration curve in a concentration range between 15 and 3000 mg/L. For our study, dilutions for calibration curves were about: 15; 60; 150; 225; 300 mg/L.

**RESULTS AND DISCUSSION**

**1. Qualitative analysis by GC-MS and Quantitative analysis with GC-FID.**

The analysis operative procedure of a sample of "Solvent Recovery" describes all the steps to carry out a testing analysis. The qualitative screening with GC-MS is fundamental to recognize all chemical compounds of the sample.

To overcome the difficulties of co-elution of different compounds, the qualitative analysis by GC-MS is fundamental for assuring the best identification, improving the quality of analytical data.

The following figures show the chromatograms obtained by GC-MS for "*Multi-standard MS-SR1*" and "*Multi-standard MS-SR2*".

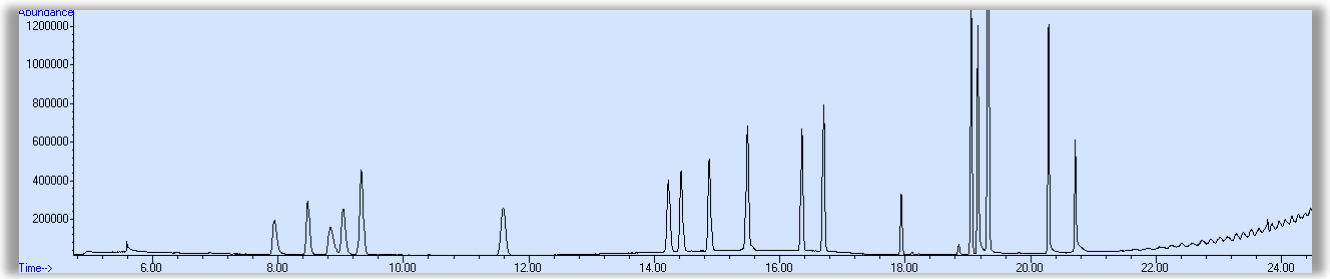



Figure 3: Chromatogram obtained by GC-MS with direct injection of "*Multi-standard MS-SR1*". The elution order from left to right is: Ethanol; Isopropanol; Acetone; Acetonitrile; Methyl acetate; Dichloromethane; Hexane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide.

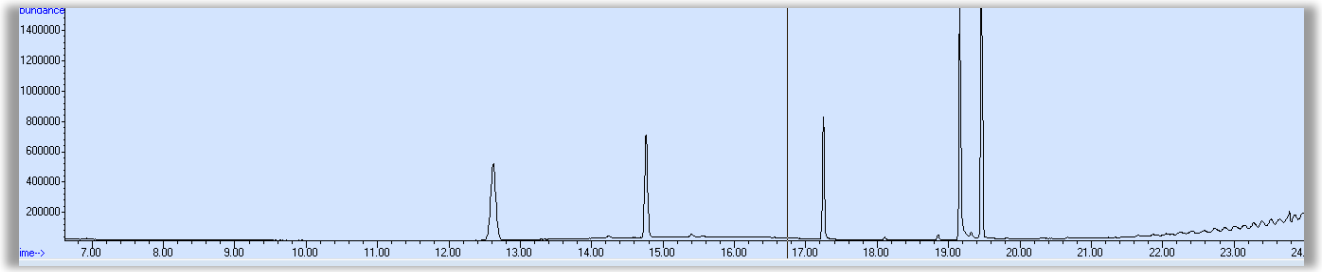



Figure 4: Chromatogram obtained with GC-MS with direct injection of for "*Multi-standard MS-SR2*".
The elution order from left to right is Diisopropyl ether; 2-Butanol; 1-Butanol; Pyridine; Octane.

The preparation of two stock solutions to calibrate the GC-MS is necessary because some compounds showed comparable retention times. If necessary, it is possible to perform the quantitative analysis by GC-MS, following the initial identification with NIST libraries.

After the screening with GC-MS, the samples can be analysed through GC-FID.

The following figures show the chromatograms of "*Multi-standard SR1*"; "*Multi-standard SR2*"and "*Multi-standard SR3*" obtained with GC-FID. The preparation of three different stock solutions, with their own calibration, is

necessary to evaluate a high number of compounds and to distinguish different peaks with the same retention time.

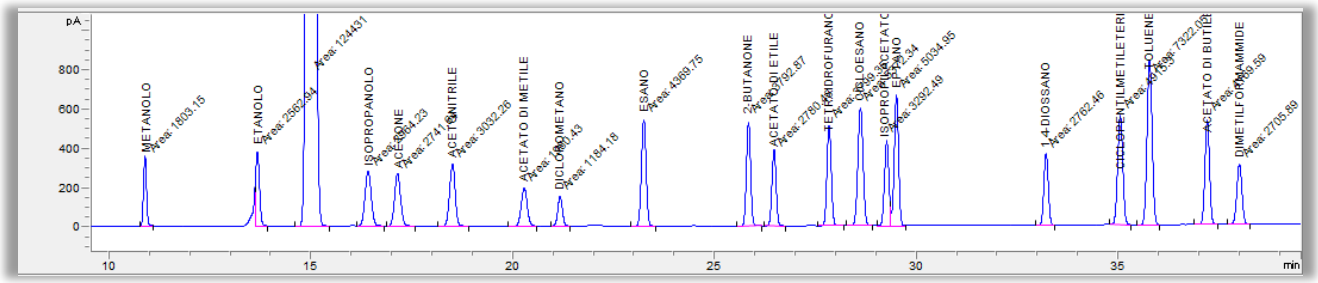



Figure 5: Chromatogram obtained with GC-FID of "*Multi-standard SR1*"

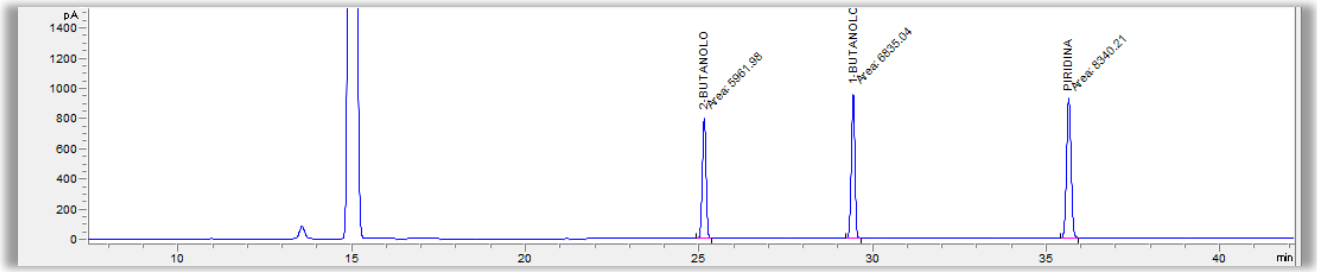



Figure 6: Chromatogram obtained with GC-FID of "*Multi-standard SR2*"

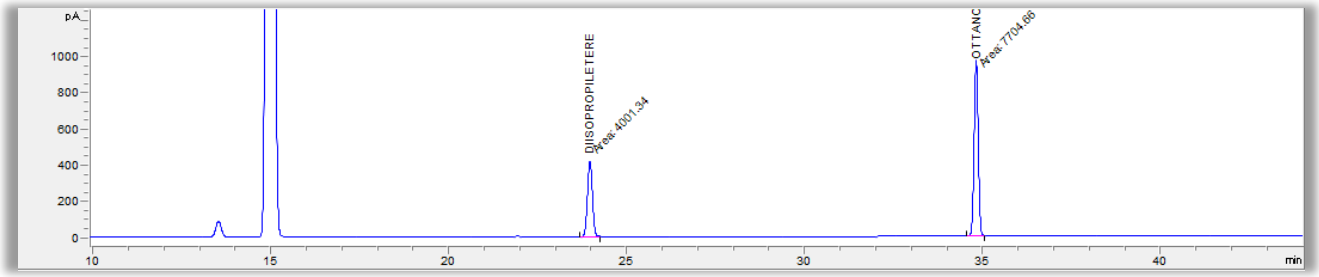



Figure 7: Chromatogram obtained with GC-FID of "*Multi-standard SR3*"

The preparation of "*Multi-standard SR1*", "*Multi-standard SR2*" and "*Multi-standard SR3*", followed during the experiments, as described in Materials and Methods, was the best manner to manage the analysis in accordance with customers' request.

**2. Calibration curves and procedures to control analytical data**

All compounds of the stock solutions ("Multistandard SR1", "Multistandard SR2","Multistandard SR3") resulted in a good linearity between the range of analysis (1000 – 30000 mg/L), as demonstrated in the calibration curves described in Appendix, section A1. This calibration, characterized by a high range of concentration, allowed the analysis of liquid waste's samples, which presented a high concentration of different solvents.

Before starting with any analytical testing, it is necessary to ensure the best instrumental performance through the execution of the "Initial Calibration Verification (ICV)" standard testing, with an acceptance range between 80-120% of the given value of the standard.

The following tables shows an example of daily quality control, performed to validate the calibration for quantitative analysis.

| COMPUNDS | RETENTION TIME (min) | CONC. STOCK SOLUTION (mg/L) | DILUTION | ICV (mg/L) | VALUE (mg/L) | RANGE (80-120)% | VALIDATION |
|---|---|---|---|---|---|---|---|
| METHANOL | 10.915 | 30024 | 1 | 15012 | 17041.7 | 113.52 | TRUE |
| ETHANOL | 13.690 | 30496 | 1 | 15248 | 18145.3 | 119.00 | TRUE |
| ISOPROPANOL | 16.466 | 29264 | 1 | 14632 | 16591 | 113.39 | TRUE |
| ACETONE | 17.166 | 29280 | 1 | 14640 | 16472.5 | 112.52 | TRUE |
| ACETONITRILE | 18.500 | 31188 | 1 | 15594 | 17651.8 | 113.20 | TRUE |
| METHYL ACETATE | 20.274 | 34616 | 1 | 17308 | 19591.3 | 113.19 | TRUE |
| DICHLOROMETANE | 21.164 | 45228 | 1 | 22614 | 25653.7 | 113.44 | TRUE |
| HEXANE | 23.240 | 25416 | 1 | 12708 | 13867.7 | 109.13 | TRUE |
| 2-BUTANONE | 25.832 | 31824 | 1 | 15912 | 17923.6 | 112.64 | TRUE |
| ETHYL ACETATE | 26.465 | 34804 | 1 | 17402 | 19581 | 112.52 | TRUE |
| TETRAHYDROFURAN | 27.831 | 33640 | 1 | 16820 | 18715.5 | 111.27 | TRUE |
| CYCLOHEXANE | 28.605 | 29724 | 1 | 14862 | 16046.8 | 107.97 | TRUE |
| ISOPROPYL ACETATE | 29.202 | 34356 | 1 | 17178 | 19103.4 | 111.21 | TRUE |
| HEPTANE | 29.501 | 26840 | 1 | 13420 | 14762.6 | 110.00 | TRUE |
| 1,4-DIOXANE | 33.203 | 39440 | 1 | 19720 | 21950.7 | 111.31 | TRUE |
| CYCLOPENTYL METHYL ETHER | 35.044 | 33528 | 1 | 16764 | 18484 | 110.26 | TRUE |
| TOLUENE | 35.771 | 33688 | 1 | 16844 | 18613.2 | 110.50 | TRUE |
| BUTYL ACETATE | 37.198 | 34412 | 1 | 17206 | 19349.5 | 112.46 | TRUE |
| DIMETHYL FORMAMIDE | 37.994 | 38540 | 1 | 19270 | 21591.3 | 112.05 | TRUE |

Table 2.: Quality control of "*Multi-standard SR1*"

| COMPUNDS | RETENTION TIME (min) | STOCK SOLUTION (mg/L) | DILUTION | ICV (mg/L) | VALUE (mg/L) | RANGE (80-120)% | VALIDATION |
|---|---|---|---|---|---|---|---|
| 2-BUTANOL | 25.136 | 30872 | 1 | 18523 | 20551.8 | 110.95 | TRUE |
| 1-BUTANOL | 29.430 | 31544 | 1 | 18926 | 21036.1 | 111.15 | TRUE |
| PYRIDINE | 35.635 | 39292 | 1 | 23575 | 24367.7 | 103.36 | TRUE |

Table 3.: Quality control of "*Multi-standard SR2*"

| COMPUNDS | RETENTION TIME (min) | STOCK SOLUTION (mg/L) | DILUTION | ICV (mg/L) | VALUE (mg/L) | RANGE (80-120)% | VALIDATION |
|---|---|---|---|---|---|---|---|
| DIISOPROPTL ETHER | 23.954 | 26992 | 1 | 13496 | 13966.5 | 103.49 | TRUE |
| OCTANE | 34.810 | 28108 | 1 | 14054 | 15886.5 | 113.04 | TRUE |

Table 4.: Quality control of "*Multi-standard SR3*"

**3. LOD and LOQ**

Limit of Detection (LOD) and Limit of Quantification (LOQ) were evaluated for the following compounds:

- Methanol; Ethanol; Acetonitrile; Hexane; Isopropanol; Methyl acetate; Dichloromethane; 2-Butanone; Ethyl acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide.

The LOD and LOQ were calculated by:

$$LOD = (3*\sigma)/k$$

$$LOQ = (10*\sigma)/k$$

where $\sigma$ is the standard deviation of peak areas and $k$ is the slope of calibration curve.

The Appendix, section A2 shows the experimental data obtained for the determination of LOD and LOQ.
The values are summarized in the following table:

| COMPOUNDS | LOD (mg/L) | LOQ (mg/L) |
|---|---|---|
| METHANOL | 31.7 | 105.7 |
| ETHANOL | 30.8 | 102.7 |
| ISOPROPANOL | 22.2 | 74.1 |
| ACETONITRILE | 37.8 | 126.0 |
| METHYL ACETATE | 31.3 | 104.4 |
| DICHLOROMETANE | 52.1 | 173.6 |
| HEXANE | 31.7 | 105.6 |
| 2-BUTANONE | 29.4 | 97.8 |
| ETHYL ACETATE | 30.6 | 102.0 |
| TETRAHYDROFURAN | 30.1 | 100.3 |
| CYCLOHEXANE | 28.2 | 94.0 |
| ISOPROPYL ACETATE | 83.0 | 276.8 |
| HEPTANE | 37.7 | 125.8 |
| 1,4-DIOXANE | 50.0 | 166.7 |
| CYCLOPENTYL-METHYL-ETHER | 28.1 | 93.7 |
| TOLUENE | 33.0 | 109.9 |
| BUTHYL ACETATE | 39.0 | 129.8 |
| N,N-DIMETHYLFORMAMIDE | 35.8 | 119.2 |

Table 5: Limit of Detection (LOD) and Limit of Quantification (LOQ)

This analytical method resulted to be adequate and it showed successful results, in terms of reliability and performance, in order to analyse "In Process Control" samples, which are important to set and control the industrial production processes. The sampling and the analysis of "In Process Control" samples, during the different steps of production, provide information about the performance of the industrial processes and support the meeting of the process specification setting.
This method was successfully applied to analyse waste solvents before and after the distillation treatment.
One of the most important product of the "Solvent Recovery" process in the industrial plant, object of this study, is pure acetone. Key important factor of the industrial distillation of pure acetone is to ensure the presence of

low impurities concentration. It is obvious that the analytical testing method needs to be capable to detect low level of impurities. This developed analytical method allows the quantification of compounds present in low concentration (0.01%) in pure acetone.

**4. Experiments of repeatability on Certified Matrix**

The performance of this analytical method was evaluated using a certified matrix.

A certified matrix with all the compounds (24) of interest for this study was not available in the market and the experiments of repeatability were carried out on a certified matrix that contained six compounds: methanol, ethanol, isopropanol, acetonitrile, ethyl acetate and toluene.

In the Appendix, the section A3 shows the experimental data of repeatability and z-*scores* obtained during the tests carried out with certified matrix.

The following tables show the summary of the results:

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **METHANOL** | **METHANOL** | **METHANOL** |
| **Spike (mg/L)** | 2531.646 | 12658.228 | 16911.392 |
| **Mean** | 2932.550 | 11408.318 | 14887.523 |
| **STD Dev.** | 63.924 | 752.898 | 1050.219 |
| **CV%** | 2.180 | 6.600 | 7.054 |
| **Recovery%_Mean** | 115.84 | 90.13 | 88.03 |
| **Recovery%_STD Dev.** | 2.52 | 5.95 | 6.21 |

Table 6: Repeatability tests carried out on Certified Matrix for Methanol

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **ETHANOL** | **ETHANOL** | **ETHANOL** |
| **Spike (mg/L)** | 2534.85 | 12674.27 | 16932.83 |
| **Mean** | 2820.206 | 12720.623 | 16082.926 |
| **STD Dev.** | 134.308 | 1084.120 | 995.123 |
| **CV%** | 4.762 | 8.523 | 6.187 |
| **Recovery%_Mean** | 111.26 | 100.37 | 94.98 |
| **Recovery%_STD Dev.** | 5.30 | 8.55 | 5.88 |

Table 7: Repeatability tests carried out on Certified Matrix for Ethanol

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **ISOPROPANOL** | **ISOPROPANOL** | **ISOPROPANOL** |
| **Spike (mg/L)** | 2544.53 | 12722.65 | 16997.46 |
| **Mean** | 2692.84 | 11457.29 | 14749.18 |
| **STD Dev.** | 153.21 | 845.65 | 1110.37 |
| **CV%** | 5.69 | 7.38 | 7.53 |
| **Recovery%_Mean** | 105.83 | 90.05 | 86.77 |
| **Recovery%_STD Dev.** | 6.02 | 6.65 | 6.53 |

Table 8: Repeatability tests carried out on Certified Matrix for Isopropanol

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **ACETONITRILE** | **ACETONITRILE** | **ACETONITRILE** |
| **Spike (mg/L)** | 2544.53 | 12722.65 | 16997.46 |
| **Mean** | 3005.816 | 10693.021 | 14239.913 |
| **STD Dev.** | 126.980 | 531.895 | 1072.346 |
| **CV%** | 4.224 | 4.974 | 7.531 |
| **Recovery%_Mean** | 118.13 | 84.05 | 83.78 |
| **Recovery%_STD Dev.** | 4.99 | 4.18 | 6.31 |

Table 9: Repeatability tests carried out on Certified Matrix for Acetonitrile

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **ETHYL ACETATE** | **ETHYL ACETATE** | **ETHYL ACETATE** |
| **Spike (mg/L)** | 2229.65 | 11148.27 | 15161.65 |
| **Mean** | 2104.141 | 10459.946 | 13410.256 |
| **STD Dev.** | 84.132 | 859.046 | 1010.877 |
| **CV%** | 3.998 | 8.213 | 7.538 |
| **Recovery%_Mean** | 94.37 | 93.83 | 88.45 |
| **Recovery%_STD Dev.** | 3.77 | 7.71 | 6.67 |

Table 10: Repeatability tests carried out on Certified Matrix for Ethyl Acetate

| | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| | **TOLUENE** | **TOLUENE** | **TOLUENE** |
| **Spike (mg/L)** | 2306.81 | 11534.03 | 15409.46 |
| **Mean** | 2524.831 | 11568.133 | 15216.345 |
| **STD Dev.** | 130.725 | 1050.384 | 1139.090 |
| **CV%** | 5.178 | 9.080 | 7.486 |
| **Recovery%_Mean** | 109.45 | 100.30 | 98.75 |
| **Recovery%_STD Dev.** | 5.67 | 9.11 | 7.39 |

Table 11: Repeatability tests carried out on Certified Matrix for Toluene

For all the compounds of certified matrix, the experiments confirmed good performance of the method.

The evaluation of *z-score* is important to evaluate the precision and accuracy of the method.

The *z-score* was calculated by:

$$z\ score = \frac{x - Xm}{\sigma}$$

where *x* is the experimental result, *Xm* is the mean value and σ is the standard deviation.

The z-*score* is considered acceptable when its value is within the range -2<*Z-score*>+2.

The Recovery is calculated as the percentage ratio between the obtained analytical result and the certified spike's value. All the values of recovery collected in these experiments were in the acceptance range between 80-120%.

The following plots show the *z-scores* associated with all the compounds of certified matrix and the percentage of recovery (Appendix, section A3).


Figure 8: Plot of z-score obtained for Level 1


Figure 9: Plot of z-score obtained for Level 2


Figure 10: Plot of z-score obtained for Level 3

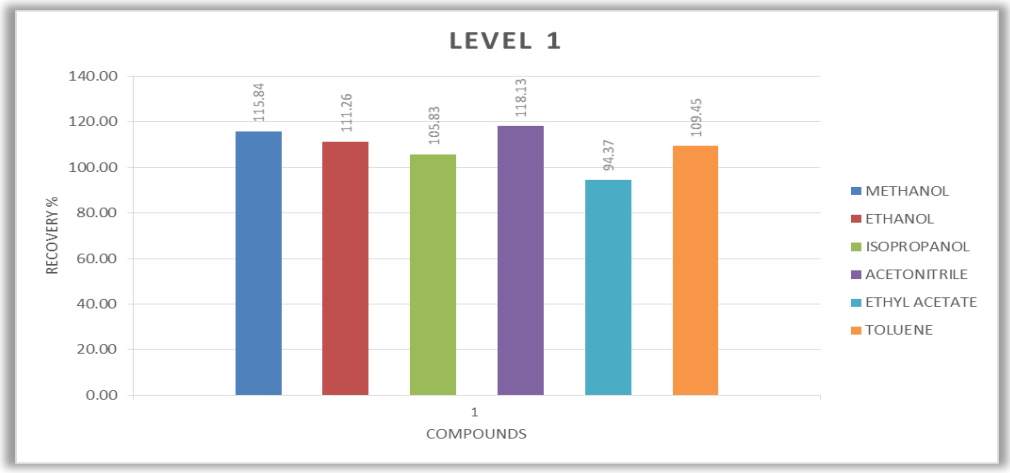



Figure 11: Percentage of Recovery obtained for Level 1

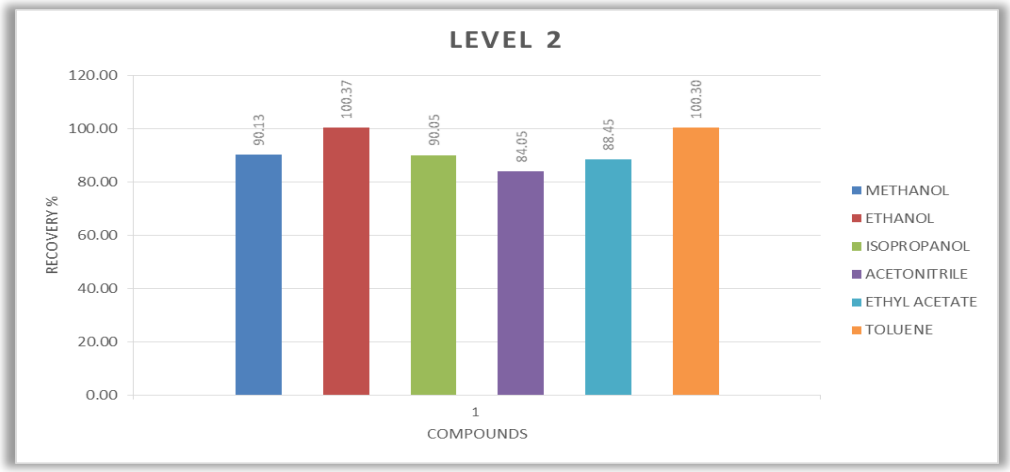



Figure 12: Percentage of Recovery obtained for Level 2

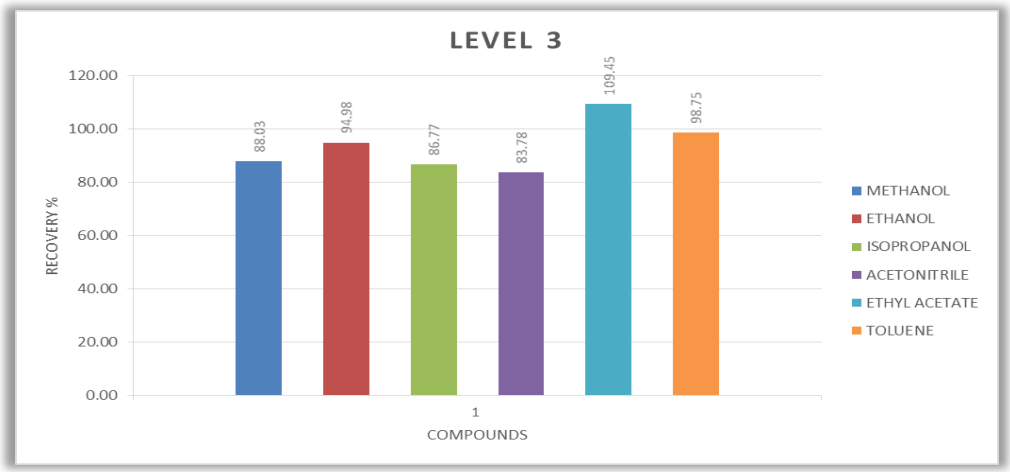



Figure 13: Percentage of Recovery obtained for Level 3

**5. Recovery of the method applied to six target compounds**

The objective of this study was the evaluation of the quality of analytical data using a statistical approach.

In this study, a particular attention was focused on the control of the recovery percentage, obtained during a long period.

The comparison between data obtained from the tests carried out on certified matrix and data obtained by daily calibration's control (ICV) gave the opportunity to demonstrate the accuracy of the analytical method.

Recovery data of ICV for six target compounds (methanol, ethanol, isopropanol, acetonitrile, ethyl acetate and toluene) were collected after 25 tests, as reported in the Appendix, section A4.

The following tables show the mean, the standard deviation and the Analysis of Variance (ANOVA) obtained for the 6 compounds under observation after 25 measures of ICV.

| **RECOVERY %** | **GROUPS** | | | | | |
|---|---|---|---|---|---|---|
| | **METHANOL** | **ETHANOL** | **ISOPROPANOL** | **ACETONITRILE** | **ETHYL ACETATE** | **TOLUENE** |
| **DIMENSION** | 25 | 25 | 25 | 25 | 25 | 25 |
| **MEAN** | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| **STD DEV.** | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |

Table 12: Mean and Standard Deviation obtained after 25 measures for methanol, ethanol, isopropanol, acetonitrile, ethyl acetate and toluene.

Analysis of Variance: one factor

RESUME

| *Groups* | *Count* | *Sum* | *Mean* | *Variance* |
|---|---|---|---|---|
| METHANOL | 25.00 | 2776.80 | 111.07 | 39.65 |
| ETHANOL | 25.00 | 2824.23 | 112.97 | 86.22 |
| ISOPROPANOL | 25.00 | 2808.59 | 112.34 | 41.61 |
| ACETONITRILE | 25.00 | 2705.53 | 108.22 | 49.02 |
| ETHYL ACETATE | 25.00 | 2776.45 | 111.06 | 30.87 |
| TOLUENE | 25.00 | 2711.49 | 108.46 | 40.38 |

ANOVA

| *Origin of the variation* | *SQ* | *Degrees of Freedom* | *MQ* | *F* | *Significancevalue* | *F crit* |
|---|---|---|---|---|---|---|
| Betweengroups | 481.99 | 5.00 | 96.40 | 2.01 | 0.08 | 3.15 |
| Withingroups | 6906.06 | 144.00 | 47.96 | | | |
| Total | 7388.05 | 149.00 | | | | |

Table 13: Test of Analysis of Variance (ANOVA)

ANOVA demonstrated that *F<F crit* and there is the same parametric variance between the groups and so the six compounds belong to the same population.

A further comparison between data obtained from certified matrix and from measures carried out on ICV is given by Z test. The Z test evaluates whether the mean for the 6 target compounds of certified matrix is closer and comparable with the mean of percentage of recovery (recovery %) obtained for ICV. The mean values of recovery for Level 1, Level 2 and Level 3 of concentration of certified matrix were compared with the mean value of recovery of ICV.

Z test was calculated by:

$$Z = \frac{X - \mu}{\sigma\sqrt{n}}$$

where $X$ is the mean value and $n$ is the number of measures (Tables 6-11); $\mu$ is the mean value and $\sigma$ is the standard deviation of a reference population of measures (Table 12).

The table below summarizes the outcome of the above-mentioned Z test.

| LEVEL 1 | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| DIMENSION | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 |
| MEAN | 115.84 | 111.26 | 105.83 | 118.13 | 94.37 | 109.45 |
| STD DEV. | 2.52 | 5.30 | 6.02 | 4.99 | 3.77 | 5.67 |
| | | | | | | |
| MEAN_Population | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| STD DEV_Population | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |
| TEST Z (Z=2.2326) | 0.29 | -0.07 | -0.38 | 0.53 | -1.14 | 0.06 |

| LEVEL 2 | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| DIMENSION | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 |
| MEAN | 90.13 | 100.37 | 90.05 | 84.05 | 93.83 | 100.30 |
| STD DEV. | 5.95 | 8.55 | 6.65 | 4.18 | 7.71 | 9.11 |
| | | | | | | |
| MEAN_Population | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| STD DEV_Population | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |
| TEST Z (Z=2.2326) | -1.26 | -0.51 | -1.31 | -1.30 | -1.17 | -0.49 |

| LEVEL 3 | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| DIMENSION | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 | 7.00 |
| MEAN | 88.03 | 94.98 | 86.77 | 83.78 | 88.45 | 98.75 |
| STD DEV. | 6.21 | 5.88 | 6.53 | 6.31 | 6.67 | 7.39 |
| | | | | | | |
| MEAN_Population | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| STD DEV_Population | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |
| TEST Z (Z=2.2326) | -1.38 | -0.73 | -1.50 | -1.32 | -1.54 | -0.58 |

Table 14: Comparison between data obtained from certificate matrix and from measures carried out on ICV by Z test

The acceptance range for Z is: $-2.2326<Z<+2.2326$ which corresponds to a significance level $\alpha=0.01$.

Test Z applied in this experiment demonstrate that a good comparison exists between the mean of the recovery % obtained with tests on certified matrix for 3 levels of concentration and the mean of the recovery % obtained from the population of ICV.

### 6. Analytical Method applied for the determination of 24 compounds

The results obtained opened the way to a development of an analytical method for the determination of 24 compounds in waste solvents and in mix of organic solvents.

The compounds of interests were:

- Methanol; Ethanol; Isopropanol; Acetone; Acetonitrile; Methyl Acetate; Dichloromethane; Hexane; 2-Butanone; Ethyl Acetate; Tetrahydrofuran; Cyclohexane; Isopropyl Acetate; Heptane; 1,4-Dioxane; Cyclopentyl methyl ether; Toluene; Butyl Acetate; N,N-Dimethylformamide; 2-Butanol; 1-Butanol; Pyridine; Diisopropylether; Octane.

These compounds are organized in three stock solutions, as described in Materials and Methods: "*Multi-standard SR1*", "*Multi-standard SR2*", and "*Multi-standard SR3*".

The Appendix, section A5 reported the results of 70 tests characterized by a population of 1680 measures of recovery of 24 compounds of interest.

The following table shows the mean and standard deviation of the distribution of the recovery (%) for 24 compounds.

| RECOVERY % | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Group 7 | Group 8 |
|---|---|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHYL ACETATE | DICHLOROMETANE | HEXANE |
| DIMENSION | 70 | 70 | 70 | 70 | 70 | 70 | 70 | 70 |
| MEAN | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 | 100.98 | 107.81 |
| STD DEV. | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 | 8.76 | 14.57 |
| CONFIDENCE 99% | 3.03 | 3.21 | 3.12 | 3.08 | 2.86 | 3.18 | 2.70 | 4.48 |
| L 1 | 95.53 | 99.20 | 95.68 | 98.59 | 97.31 | 99.54 | 98.98 | 104.17 |
| L 2 | 101.60 | 103.89 | 100.46 | 103.06 | 101.46 | 104.31 | 102.97 | 111.45 |
| LCL | 95.03 | 97.80 | 94.44 | 97.24 | 96.05 | 98.22 | 97.84 | 102.58 |
| UCL | 102.10 | 105.29 | 101.71 | 104.41 | 102.72 | 105.64 | 104.12 | 113.03 |

| RECOVERY % | Group 9 | Group 10 | Group 11 | Group 12 | Group 13 | Group 14 | Group 15 | Group 16 |
|---|---|---|---|---|---|---|---|---|
| | 2-BUTANONE | ETHYL ACETATE | TETRAHYDROFURAN | CYCLOHEXANE | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER |
| DIMENSION | 70 | 70 | 70 | 70 | 70 | 70 | 70 | 70 |
| MEAN | 99.16 | 100.07 | 100.15 | 109.79 | 99.68 | 101.90 | 98.30 | 101.14 |
| STD DEV. | 8.77 | 10.22 | 8.65 | 24.73 | 10.68 | 18.66 | 9.50 | 8.27 |
| CONFIDENCE 99% | 2.70 | 3.15 | 2.66 | 7.61 | 3.29 | 5.75 | 2.93 | 2.55 |
| L 1 | 96.99 | 97.72 | 98.19 | 104.04 | 97.09 | 97.64 | 96.03 | 99.23 |
| L 2 | 101.33 | 102.42 | 102.11 | 115.55 | 102.26 | 106.16 | 100.58 | 103.04 |
| LCL | 96.02 | 96.40 | 97.05 | 100.93 | 95.85 | 95.21 | 94.90 | 98.17 |
| UCL | 102.31 | 103.73 | 103.25 | 118.66 | 103.51 | 108.59 | 101.71 | 104.10 |

| RECOVERY % | Group 17 | Group 18 | Group 19 | Group 20 | Group 21 | Group 22 | Group 23 | Group 24 |
|---|---|---|---|---|---|---|---|---|
| | TOLUENE | BUTHYL ACETATE | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
| DIMENSION | 70 | 70 | 70 | 70 | 70 | 70 | 70 | 70 |
| MEAN | 101.34 | 99.99 | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV. | 8.45 | 9.36 | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| CONFIDENCE 99% | 2.60 | 2.88 | 2.99 | 3.62 | 3.74 | 3.02 | 3.11 | 3.85 |
| L 1 | 99.37 | 97.79 | 97.67 | 97.41 | 95.32 | 95.79 | 93.31 | 94.83 |
| L 2 | 103.32 | 102.20 | 102.07 | 102.74 | 102.71 | 101.76 | 99.32 | 101.39 |
| LCL | 98.31 | 96.64 | 96.39 | 95.86 | 94.65 | 95.26 | 92.69 | 93.62 |
| UCL | 104.37 | 103.35 | 103.35 | 104.30 | 103.38 | 102.29 | 99.94 | 102.60 |

Table 15: Mean and Standard Deviation of the population of 70 tests characterized by a population of 1680 measures of recovery % of 24 compounds of interest

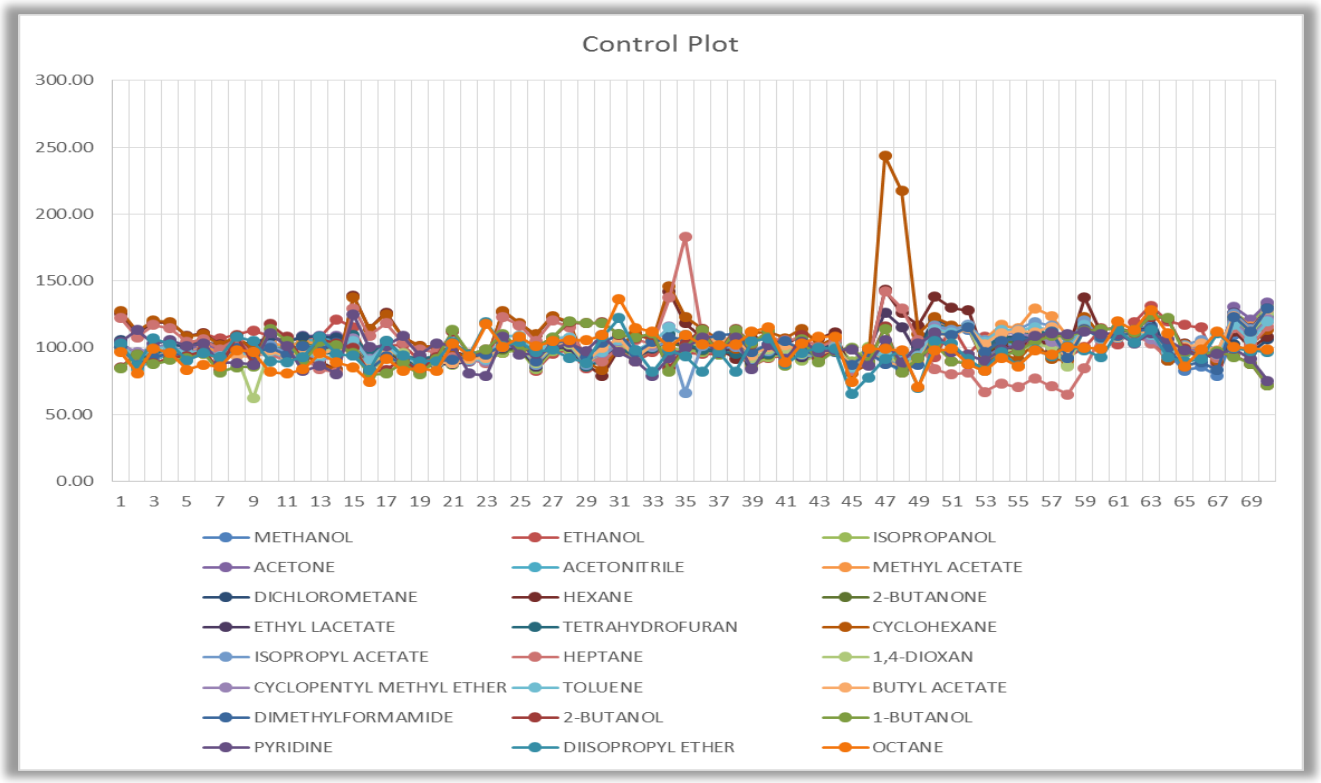



Figure 14: Flow Chart to control recovery % of 24 analytes

These measures gave a normal distribution of recovery for 24 compounds. A flow chart (Figure 14) is used to evaluate the fluctuations of the values around the mean value.

By reviewing the plot, it is possible to evaluate the presence of any outliers for very few compounds.

It is important to know the value of Lower Control Limit (LCL) and of the Upper Control Limit (UCL) obtained by:

$$LCL = X - \alpha \frac{\sigma}{\sqrt{n}}$$

$$UCL = X + \alpha \frac{\sigma}{\sqrt{n}}$$

The application of test of ANOVA demonstrates that, in this case, the total variance is not representative for all compounds.

The Appendix, section A5 shows the experimental data obtained for the determination of recovery.

Analysis of Variance; one factor

Resume

| *Groups* | *Count* | *Sum* | *Mean* | *Variance* |
|---|---|---|---|---|
| METHANOL | 70 | 6899.58 | 98.57 | 97.04 |
| ETHANOL | 70 | 7108.16 | 101.55 | 108.88 |
| ISOPROPANOL | 70 | 6865.18 | 98.07 | 102.75 |
| ACETONE | 70 | 7057.76 | 100.83 | 100.01 |
| ACETONITRILE | 70 | 6957.05 | 99.39 | 86.58 |
| METHYL ACETATE | 70 | 7134.89 | 101.93 | 106.96 |
| DICHLOROMETANE | 70 | 7068.49 | 100.98 | 76.70 |
| HEXANE | 70 | 7546.46 | 107.81 | 212.20 |
| 2-BUTANONE | 70 | 6941.48 | 99.16 | 76.93 |
| ETHYL LACETATE | 70 | 7004.76 | 100.07 | 104.51 |
| TETRAHYDROFURAN | 70 | 7010.44 | 100.15 | 74.89 |
| CYCLOHEXANE | 70 | 7685.53 | 109.79 | 611.65 |
| ISOPROPHYL ACETATE | 70 | 6977.39 | 99.68 | 114.06 |
| HEPTANE | 70 | 7132.90 | 101.90 | 348.33 |
| 1,4-DIOXAN | 70 | 6881.19 | 98.30 | 90.29 |
| CYCLOPENTYL METHYL ETHER | 70 | 7079.49 | 101.14 | 68.42 |
| TOLUENE | 70 | 7094.08 | 101.34 | 71.41 |
| BUTHYL ACETATE | 70 | 6999.64 | 99.99 | 87.68 |
| DIMETHYLFORMAMIDE | 70 | 6990.96 | 99.87 | 94.08 |
| 2-BUTANOL | 70 | 7005.40 | 100.08 | 138.38 |
| 1-BUTANOL | 70 | 6931.05 | 99.02 | 147.86 |
| PYRIDINE | 70 | 6914.29 | 98.78 | 96.23 |
| DIISOPROPYL ETHER | 70 | 6741.96 | 96.31 | 102.07 |
| OCTANE | 70 | 6867.59 | 98.11 | 156.73 |

ANALYSIS OF VARIANCE

| *Origin of variazione* | *SQ* | *Degrees of Freedom* | *MQ* | *F* | *Significance Value* | *F crit* |
|---|---|---|---|---|---|---|
| BetweenGroups | 13578.63 | 23 | 590.38 | 4.33 | 0.00 | 1.82 |
| WithinGroups | 225950.12 | 1656 | 136.44 | | | |
| Total | 239528.76 | 1679 | | | | |

Table 16: Test of Analysis of Variance (ANOVA) applied to all 24 compounds

In this ANOVA, F>Fcrit and the different compounds belong to different populations.

The ANOVA allows the classification of the compounds in three groups to explain the total variance:

- Recovery % less than 100
- Recovery % closer to 100
- Recovery higher than 100

ANOVA tests were applied to classify these populations in which F<Fcrit.

Analysis of Variance; one factor

Resume

| *Groups* | *Count* | *Sum* | *Mean* | *Variance* |
|---|---|---|---|---|
| METHANOL | 70 | 6899.58 | 98.57 | 97.04 |
| ISOPROPANOL | 70 | 6865.18 | 98.07 | 102.75 |
| 1,4-DIOXAN | 70 | 6881.19 | 98.30 | 90.29 |
| PYRIDINE | 70 | 6914.29 | 98.78 | 96.23 |
| DIISOPROPYL ETHER | 70 | 6741.96 | 96.31 | 102.07 |
| OCTANE | 70 | 6867.59 | 98.11 | 156.73 |

ANALYSIS OF VARIANCE

| *Origin of variation* | *SQ* | *Degrees of Freedom* | *MQ* | *F* | *Significance Value* | *F crit* |
|---|---|---|---|---|---|---|
| BetweenGroups | 270.91 | 5 | 54.18 | 0.50 | 0.77 | 3.06 |
| WithinGroups | 44512.61 | 414 | 107.52 | | | |
| Total | 44783.52 | 419 | | | | |

Table 17: ANOVA test for compounds that showed the mean of Recovery less than 100%

Analysis of Variance; one factor

Resume

| *Groups* | *Count* | *Sum* | *Mean* | *Variance* |
|---|---|---|---|---|
| ETHANOL | 70 | 7108.16 | 101.55 | 108.88 |
| ACETONE | 70 | 7057.76 | 100.83 | 100.01 |
| ACETONITRILE | 70 | 6957.05 | 99.39 | 86.58 |
| METHYL ACETATE | 70 | 7134.89 | 101.93 | 106.96 |
| DICHLOROMETANE | 70 | 7068.49 | 100.98 | 76.70 |
| 2-BUTANONE | 70 | 6941.48 | 99.16 | 76.93 |
| ETHYL LACETATE | 70 | 7004.76 | 100.07 | 104.51 |
| TETRAHYDROFURAN | 70 | 7010.44 | 100.15 | 74.89 |
| ISOPROPHYL ACETATE | 70 | 6977.39 | 99.68 | 114.06 |
| HEPTANE | 70 | 7132.90 | 101.90 | 348.33 |
| CYCLOPENTYL METHYL ETHER | 70 | 7079.49 | 101.14 | 68.42 |
| TOLUENE | 70 | 7094.08 | 101.34 | 71.41 |
| BUTHYL ACETATE | 70 | 6999.64 | 99.99 | 87.68 |
| DIMETHYLFORMAMIDE | 70 | 6990.96 | 99.87 | 94.08 |
| 2-BUTANOL | 70 | 7005.40 | 100.08 | 138.38 |
| 1-BUTANOL | 70 | 6931.05 | 99.02 | 147.86 |

ANALYSIS OF VARIANCE

| *Origin of variation* | *SQ* | *Degrees of Freedom* | *MQ* | *F* | *Significance Value* | *F crit* |
|---|---|---|---|---|---|---|
| BetweenGroups | 946.84 | 15 | 63.12 | 0.56 | 0.91 | 2.05 |
| WithinGroups | 124591.99 | 1104 | 112.86 | | | |
| Total | 125538.83 | 1119 | | | | |

Table 18: ANOVA test for compounds that showed the mean of Recovery closer to 100%

Analysis of Variance; one factor

Resume

| *Groups* | *Count* | *Sum* | *Mean* | *Variance* |
|---|---|---|---|---|
| HEXANE | 70 | 7546.46 | 107.81 | 212.20 |
| CYCLOHEXANE | 70 | 7685.53 | 109.79 | 611.65 |

ANALYSIS OF VARIANCE

| *Origin of variation* | *SQ* | *Degrees of Freedom* | *MQ* | *F* | *Significance Value* | *F crit* |
|---|---|---|---|---|---|---|
| BetweenGroups | 138.15 | 1 | 138.15 | 0.34 | 0.56 | 6.82 |
| WithinGroups | 56845.53 | 138 | 411.92 | | | |
| Total | 56983.68 | 139 | | | | |

Table 19: ANOVA test for compounds that showed the mean of Recovery higher than 100%

| Recovery less than 100 % | Recovery closer to 100 % | Recovery higher than 100 % |
|---|---|---|
| METHANOL | ETHANOL | HEXANE |
| ISOPROPANOL | ACETONE | CYCLOHEXANE |
| 1,4-DIOXAN | ACETONITRILE | |
| PYRIDINE | METHYL ACETATE | |
| DIISOPROPYL ETHER | DICHLOROMETANE | |
| OCTANE | 2-BUTANONE | |
| | ETHYL LACETATE | |
| | TETRAHYDROFURAN | |
| | ISOPROPHYL ACETATE | |
| | HEPTANE | |
| | CYCLOPENTYL METHYL ETHER | |
| | TOLUENE | |
| | BUTHYL ACETATE | |
| | DIMETHYLFORMAMIDE | |
| | 2-BUTANOL | |
| | 1-BUTANOL | |

| Mean of Recovery %_1 | Mean of Recovery %_2 | Mean of Recovery %_3 |
|---|---|---|
| 98.02 | 100.44 | 108.80 |
| **STD Dev of Recovery %_1** | **STD Dev of Recovery %_2** | **STD Dev of Recovery %_3** |
| 1.10 | 2.49 | 7.19 |

Table 20: Classification of all compounds based on ANOVA applied to recovery values.

### 7. Reproducibility Experiments

Experiments to evaluate the reproducibility of analytical data were carried out through the analysis of ICV with two different instruments GC-FID (called "*GC-FID_Principal*" and "*GC-FID_Control*"). The "*GC-FID_Principal*" was considered as the principal instrument for all the tests and the "*GC-FID_Control*" was used to compare the series of analytical data.

The ICV were analysed with "*GC-FID_Principal*" and "*GC-FID_Control*" to generate two series of recovery % of seven data for each compound. The Appendix, section A6 shows the complete population of data.

The Test Z applied to both series of the data demonstrated that they were representative of the population of recovery data of 24 compounds, as described in paragraph 6 and in Appendix, section A5.

According with the formula of Test Z:

$$Z = \frac{X - \mu}{\sigma\sqrt{n}}$$

where μ and σ were respectively the mean and the standard deviation of the entire population of recovery data; X was the mean of the two series of measures of recovery and *n* is the number of measures.

The comparison between data of the two instruments was described in term of Bravais' coefficient R:

$$R = \frac{\sum(xi - mean(x)) * (yi - mean(y))}{\sqrt{\sum (xi - mean(x))\text{^}2 * \sum(yi - mean(y))\text{^}2}}$$

The following tables show the results obtained in term of mean and standard deviation:

| GC-FID_Control | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHYLACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 98.81 | 99.83 | 99.97 | 102.05 | 100.19 | 98.65 |
| STANDARD DEVIATION | 11.27 | 14.42 | 14.64 | 11.51 | 13.82 | 9.97 |
| | | | | | | |
| MEAN_all | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 |
| STD DEV_all | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 |
| TEST Z (Z=2.2326) | 0.01 | -0.06 | 0.07 | 0.05 | 0.03 | -0.12 |

| GC-FID_Control | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 102.93 | 98.80 | 95.89 | 99.83 | 87.32 | 100.22 |
| STANDARD DEVIATION | 10.26 | 13.62 | 17.87 | 10.82 | 23.47 | 13.86 |
| | | | | | | |
| MEAN_all | 100.98 | 107.81 | 99.16 | 100.07 | 100.15 | 109.79 |
| STD DEV_all | 8.76 | 14.57 | 8.77 | 10.22 | 8.65 | 24.73 |
| TEST Z (Z=2.2326) | 0.08 | -0.23 | -0.14 | -0.01 | -0.56 | -0.15 |

| GC-FID_Control | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 101.67 | 101.21 | 100.09 | 101.46 | 101.11 | 100.69 |
| STANDARD DEVIATION | 11.89 | 12.64 | 11.21 | 7.93 | 8.25 | 12.17 |
| | | | | | | |
| MEAN_all | 99.68 | 101.90 | 98.30 | 101.14 | 101.34 | 99.99 |
| STD DEV_all | 10.68 | 18.66 | 9.50 | 8.27 | 8.45 | 9.36 |
| TEST Z (Z=2.2326) | 0.07 | -0.01 | 0.07 | 0.01 | -0.01 | 0.03 |

| GC-FID_Control | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 101.16 | 96.99 | 97.54 | 94.78 | 101.68 | 102.58 |
| STANDARD DEVIATION | 13.37 | 22.20 | 22.74 | 8.68 | 13.07 | 12.89 |
| | | | | | | |
| MEAN_all | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV_all | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| TEST Z (Z=2.2326) | 0.05 | -0.10 | -0.05 | -0.15 | 0.20 | 0.14 |

Table 21: Results of reproducibility test for 24 compounds obtained by "*GC-FID_Control*"

| GC-FID_Principal | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 98.55 | 104.83 | 95.42 | 101.61 | 97.75 | 99.49 |
| STANDRD DEVIATION | 7.24 | 9.13 | 7.25 | 7.82 | 7.72 | 5.86 |
| | | | | | | |
| MEAN_all | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 |
| STD DEV_all | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 |
| TEST Z (Z=2.2326) | 0.00 | 0.12 | -0.10 | 0.03 | -0.07 | -0.09 |

| GC-FID_Principal | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 102.70 | 106.87 | 96.63 | 95.24 | 97.52 | 106.35 |
| STANDRD DEVIATION | 6.69 | 17.86 | 5.55 | 5.21 | 5.56 | 18.35 |
| | | | | | | |
| MEAN_all | 100.98 | 107.81 | 99.16 | 100.07 | 100.15 | 109.79 |
| STD DEV_all | 8.76 | 14.57 | 8.77 | 10.22 | 8.65 | 24.73 |
| TEST Z (Z=2.2326) | 0.07 | -0.02 | -0.11 | -0.18 | -0.11 | -0.05 |

| GC-FID_Principal | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 95.30 | 102.35 | 89.78 | 96.00 | 95.66 | 93.42 |
| STANDRD DEVIATION | 6.19 | 16.58 | 13.12 | 5.70 | 5.05 | 4.53 |
| | | | | | | |
| MEAN_all | 99.68 | 101.90 | 98.30 | 101.14 | 101.34 | 99.99 |
| STD DEV_all | 10.68 | 18.66 | 9.50 | 8.27 | 8.45 | 9.36 |
| TEST Z (Z=2.2326) | -0.16 | 0.01 | -0.34 | -0.23 | -0.25 | -0.27 |

| GC-FID_Principal | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 94.29 | 93.67 | 91.83 | 94.90 | 96.45 | 87.68 |
| STANDRD DEVIATION | 5.70 | 9.99 | 9.51 | 8.97 | 9.95 | 9.60 |
| | | | | | | |
| MEAN_all | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV_all | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| TEST Z (Z=2.2326) | -0.22 | -0.21 | -0.22 | -0.15 | 0.00 | -0.31 |

Table 22: Results of reproducibility test for 24 compounds obtained by "*GC-FID_Principal*"

The following plots shows the mean recovery obtained by "*GC-FID_Control*" and "*GC-FID_Principal*"

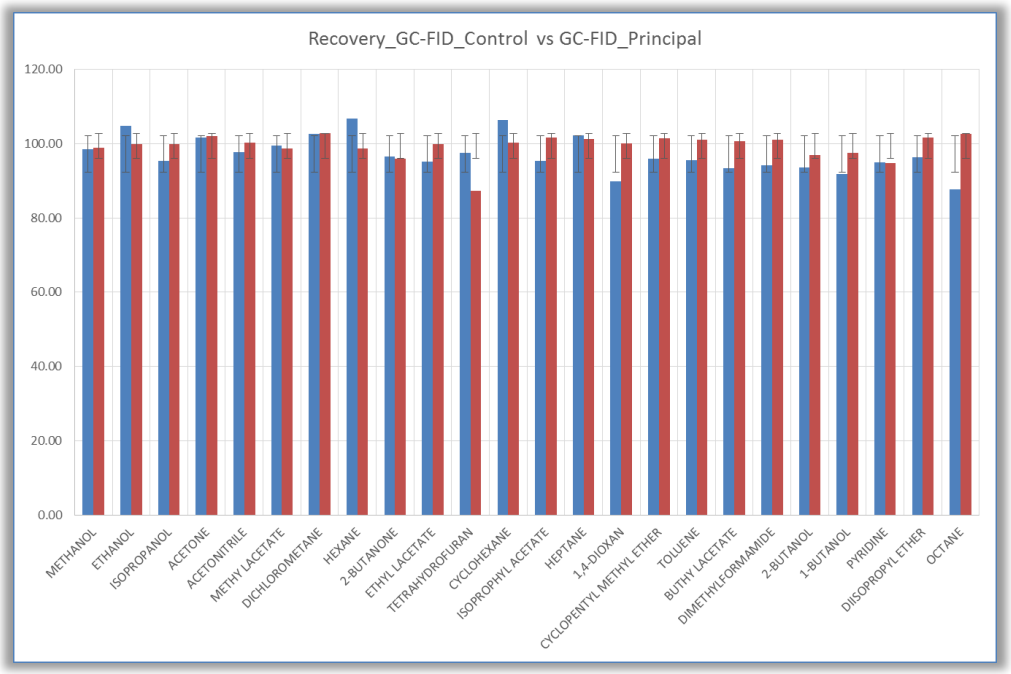



Figure 15: Comparison between recovery obtained with GC-FID_Control (Red) and GC-FID_Principal (Blue).

| | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE | DICHLOROMETANE | HEXANE |
|---|---|---|---|---|---|---|---|---|
| BRAVAIS_R | 0.59 | 0.16 | 0.79 | 0.68 | 0.74 | 0.44 | 0.59 | 0.79 |

| | ETHYL ACETATE | TETRAHYDROFURAN | CYCLOHEXANE | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER |
|---|---|---|---|---|---|---|---|
| BRAVAIS_R | 0.56 | -0.46 | 0.82 | 0.61 | 0.83 | 0.63 | 0.04 |

| | BUTHY LACETATE | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
|---|---|---|---|---|---|---|---|
| BRAVAIS_R | 0.54 | 0.72 | 0.73 | 0.73 | -0.72 | 0.38 | 0.23 |

Table 23: Test of Bravais for comparison of recovery obtained through analytical data from two instruments

The results obtained showed the existence of reproducibility of analytical recoveries for all compounds.

## 8. Experiments on matrix spiked

This study was focused to evaluate the quality of analytical data for the method used and the tests were carried out on standard solutions. It is important to evaluate the data in the case of a real matrix to evaluate how matrix can affect the analysis.

Matrix effects can be detected comparing a Laboratory Control Sample (LCS) with Matrix (M), Matrix Spike (MS) and Matrix Spike Duplicate (MSD). The LCS, MS and MSD were characterized by similar concentration to evaluate the difference between recoveries: the composition of a real matrix could affect the quality of analytical data. These experiments had the objective to verify that analytical data obtained from real matrices were under control in a specific range of acceptance 70-130%. This range is a little different from ICV's acceptability (80-120%) because of the matrix effects. Real matrices were spiked with a low concentration of standard and were analysed to evaluate recovery of all compounds of interest. In these experiments, the spike was made with six target compounds: methanol, ethanol, isopropanol, acetonitrile, ethyl acetate and toluene.

The Appendix, section A7 shows the results obtained in all tests carried out on LCS, M, MS and MSD.

The following tables show the results

| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| DIMENSION | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| AVERAGE VALUE | 107.34 | 113.80 | 105.61 | 100.56 | 105.28 | 104.21 |
| STANDRD DEVIATION | 11.14 | 9.94 | 9.86 | 10.22 | 8.10 | 10.81 |
| RSD% | 10.37 | 8.73 | 9.34 | 10.16 | 7.70 | 10.37 |

Table 24: Recovery for LCS obtained after 20 tests

| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| DIMENSION | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| AVERAGE VALUE | 117.28 | 120.87 | 117.07 | 115.78 | 84.59 | 113.79 |
| STANDRD DEVIATION | 24.82 | 20.42 | 25.82 | 25.61 | 18.62 | 26.32 |
| RSD % | 21.16 | 16.89 | 22.05 | 22.12 | 22.02 | 23.13 |

Table 25: Recovery for MS obtained after 20 tests

| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| DIMENSION | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| AVERAGE VALUE | 116.91 | 122.61 | 118.45 | 115.59 | 85.60 | 114.45 |
| STANDRD DEVIATION | 24.26 | 17.85 | 24.15 | 24.59 | 16.96 | 24.52 |
| RSD % | 20.75 | 14.56 | 20.39 | 21.27 | 19.81 | 21.42 |

Table 26: Recovery for MSD obtained after 20 tests

MS, MSD and LCS showed that recovery are acceptable for analysis and the method was successfully applied for the analysis of real matrices.

**CONCLUSIONS**

The topic of this work was the development of an analytical method for the determination of volatile organic compounds (VOC) in waste recovered solvents from a pharmaceutical manufacturing plant.

This analytical method was developed in compliance with official method EPA 8015D and shows some advantage in term of specificity and reduction of time analysis.

In this work new compounds, other than those listed in official method EPA 8015D, were introduced:

- Methyl Acetate
- Dichloromethane
- Hexane
- Tetrahydrofuran
- Cyclohexane
- Isopropyl Acetate
- Heptane
- 1,4-Dioxane
- Cyclopentyl Methyl Ether
- Butyl Acetate
- N,N-Dimethylformamide
- 2-Butanol
- 1-Butanol
- Octane

The results obtained in this work demonstrated the validity of the analytical conditions for all examinated compounds. Official method EPA 8015D is restricted to no halogenated organic compounds, but this study showed good results also for dichloromethane.

The pentane was a good solvent for all compounds and its peak appeared separated from all compounds of interest. In this method the use of a column with a length of 60 m, as an alternative to those recommended in the method EPA 8015D with a length of 30m, showed a good chromatographic separation and it was preferential for the application of the method for the determination of numerous compounds.

This new approach with analysis of samples of waste and recovered solvents is according with customer's requests who are looking for laboratories able to analyse complex matrices,with the presence of a high number of molecules present in different concentration, reducing time and costs.

The synergic use of GC-MS with headspace injection, or direct injection, for qualitative analysis and GC-FID for quantitative analysis allowed the development of a method with advantages in term of specific identification and the quantification of different molecules.

This developed analytical method was successfully applied for VOC determination in waste and recovered solvents and it is very useful in the "Solvent Recovery" plant to control processes and to make correlations between the composition of different matrices (waste solvents, recovered solvents and wastewaters). Quantitative approach with GC-FID allows to determinate the composition of samples of waste solvents, products "in process" and final products (pure solvents or mixture).

The following table shows some typical determinations of different compounds in waste and recovered solvents.

Waste solvents are complex matrices with different compound, while recovered solvents are matrices characterized by purified mix or pure solvents.

| | **Waste Solvents_sample 1** | **Waste Solvents_sample 2** | **Waste Solvents_sample 3** | **Waste Solvents_sample 4** |
|---|---|---|---|---|
| **COMPOUNDS** | **mg/L** | **mg/L** | **mg/L** | **mg/L** |
| METHANOL | 13059.9 | 6989.15 | 123472 | 84511.30 |
| ETHANOL | | | 28529.4 | 53067.1 |
| ISOPROPANOL | 12543.1 | | 19728.2 | 62288.2 |
| ACETONE | 27174 | 315613 | 203656 | 145403 |
| ACETONITRILE | | | 10105.7 | 18379.2 |
| METHYL ACETATE | | 260997 | 39022.1 | |
| DICHLOROMETANE | | 3582.7 | 57654.9 | 20241.8 |
| HEXANE | | | | |
| 2-BUTANONE | | | 1023.08 | |
| ETHYL LACETATE | 1469.12 | 2480.34 | 121236 | 185996 |
| TETRAHYDROFURAN | 13227.2 | | 16725.9 | 11616.5 |
| CYCLOHEXANE | | | | 3551.98 |
| ISOPROPYL ACETATE | | | 10046.4 | 5317.89 |
| HEPTANE | | | | 503.13 |
| 1,4-DIOXAN | | | | |
| CYCLOPENTYL METHYL ETHER | | | | |
| TOLUENE | 7595.8 | | 76645.5 | 102757 |
| BUTYL ACETATE | | | | |
| DIMETHYLFORMAMIDE | | | | |
| 2-BUTANOL | 12799.1 | | | |
| 1-BUTANOL | | | | |
| PYRIDINE | | | | |
| DIISOPROPYL ETHER | | | 1392.67 | |
| OCTANE | | | | |
| **Totals (mg/L)** | 87868.22 | 589662.19 | 709237.85 | 693633.10 |

Table n. 27: Typical composition of waste solvents

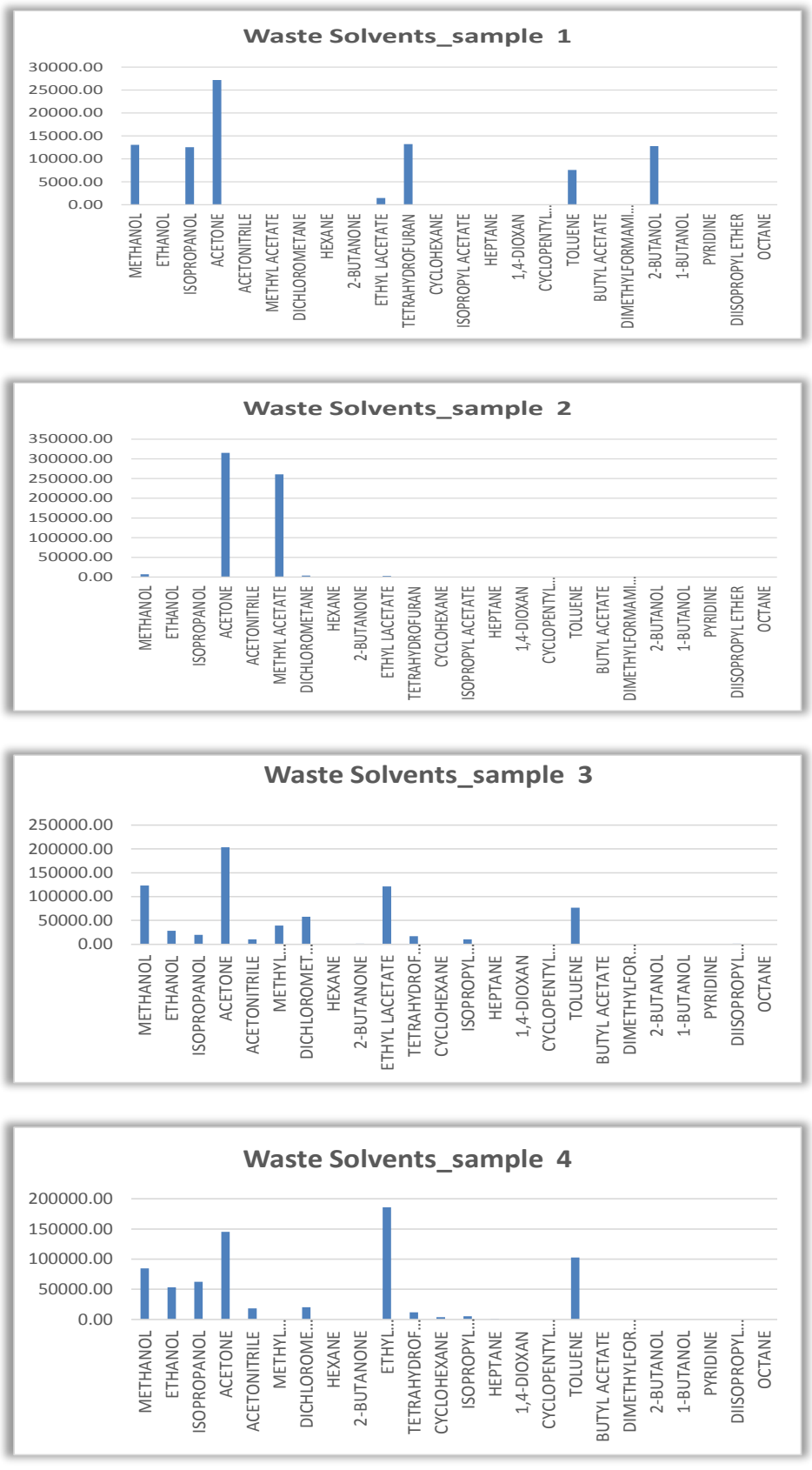



Figure 16: Plots of the compositions of 4 samples of waste solvents

| | Recovered Solvents_sample 1 | Recovered Solvents_sample 2 | Recovered Solvents_sample 3 | Recovered Solvents_sample 4 |
|---|---|---|---|---|
| **COMPOUNDS** | **mg/L** | **mg/L** | **mg/L** | **mg/L** |
| METHANOL | 164545 | | 36406.5 | 6781.24 |
| ETHANOL | 193499 | | | 867.8 |
| ISOPROPANOL | 77157.1 | 163325 | 12566 | |
| ACETONE | 6679.08 | 225132 | 65806.8 | 804158 |
| ACETONITRILE | | | | |
| METHYL ACETATE | | | | |
| DICHLOROMETANE | | | 15180.8 | |
| HEXANE | | | | |
| 2-BUTANONE | | | | |
| ETHYL LACETATE | 21570 | | 562348 | 4930.53 |
| TETRAHYDROFURAN | | | 878.05 | |
| CYCLOHEXANE | 5479.53 | 1835.52 | | |
| ISOPROPYL ACETATE | | | | |
| HEPTANE | | | | |
| 1,4-DIOXAN | | | | |
| CYCLOPENTYL METHYL ETHER | | | | |
| TOLUENE | 25419.7 | 188737 | 2863.1 | |
| BUTYL ACETATE | | | 2472.43 | |
| DIMETHYLFORMAMIDE | | | | |
| 2-BUTANOL | | | | 63791.7 |
| 1-BUTANOL | | | | |
| PYRIDINE | | | | |
| DIISOPROPYL ETHER | | | | |
| OCTANE | | | | |
| **Totals (mg/L)** | 494349.41 | 579029.52 | 698521.68 | 880529.27 |

Table n. 28: Typical composition of recovered solvents

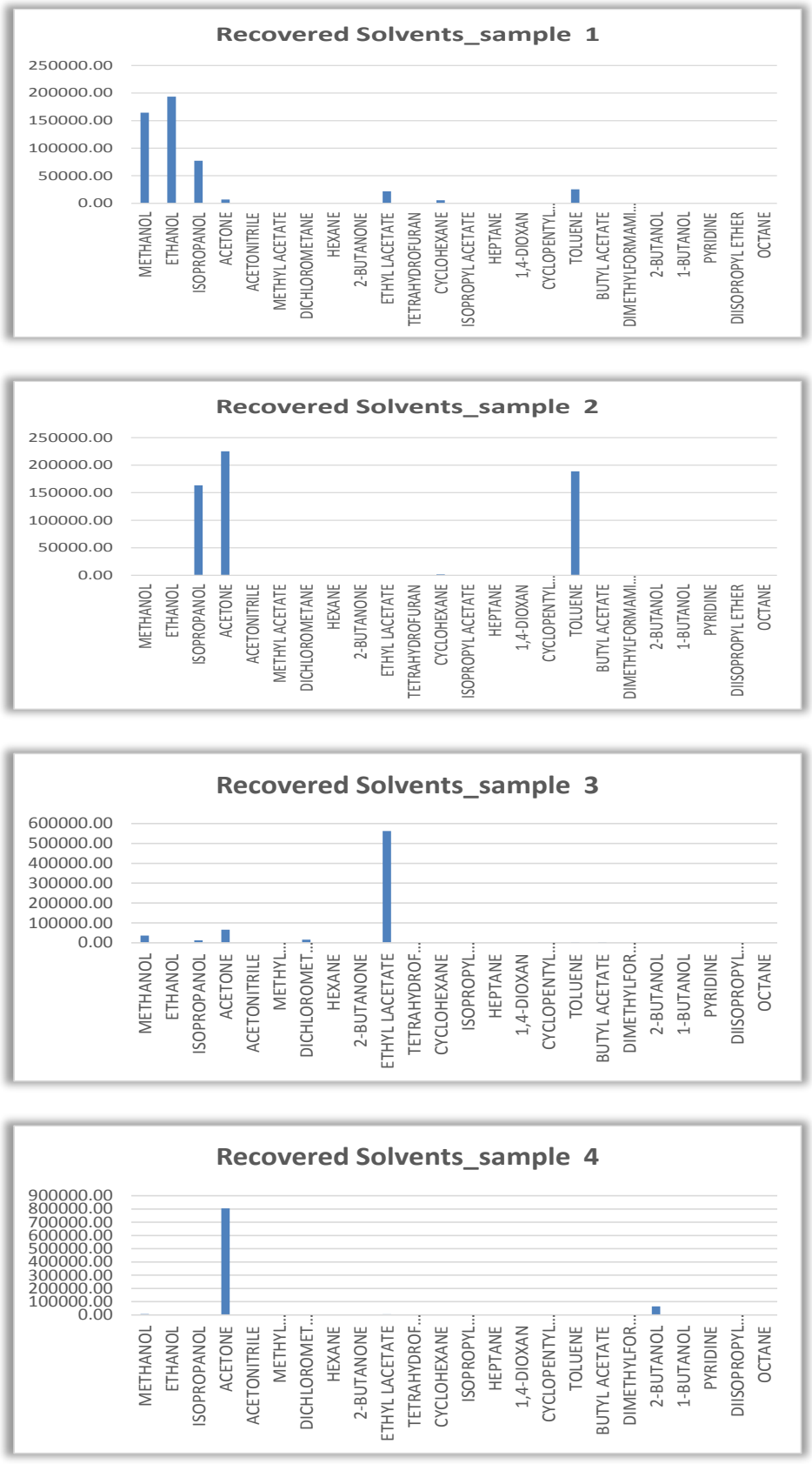



Figure 17: Plots of the compositions of 4 samples of recovered solvents

This method is successfully applied for many industrial implications:

- the analysis of waste solvents is important for the characterization of the samples and to assure the compliance with laws
- the analysis of products "in process" plays a pivotal role for the control of the efficiency of the separation: for example the analysis could put in evidence the presence of azeotropes during the distillation
- the analysis of the final products is determinant for the distribution of the product on the market
- the analysis of waste of production, for example a wastewater with a high concentration of solvents before the depuration, is important to control the pre-treatment to reduce the solvent's content in wastewater and to preserve the industrial depurator
- this method allows to execute analysis in a short time in accordance with industrial needs to have an immediate control of all the steps of the processes.

Future developments of this analytical method are always opened to determination of different compounds, for example: tert-butanol, hexamethyldisiloxane, triethylamine, methyl isobutyl ketone, o-xylene, m-xylene, p-xylene.

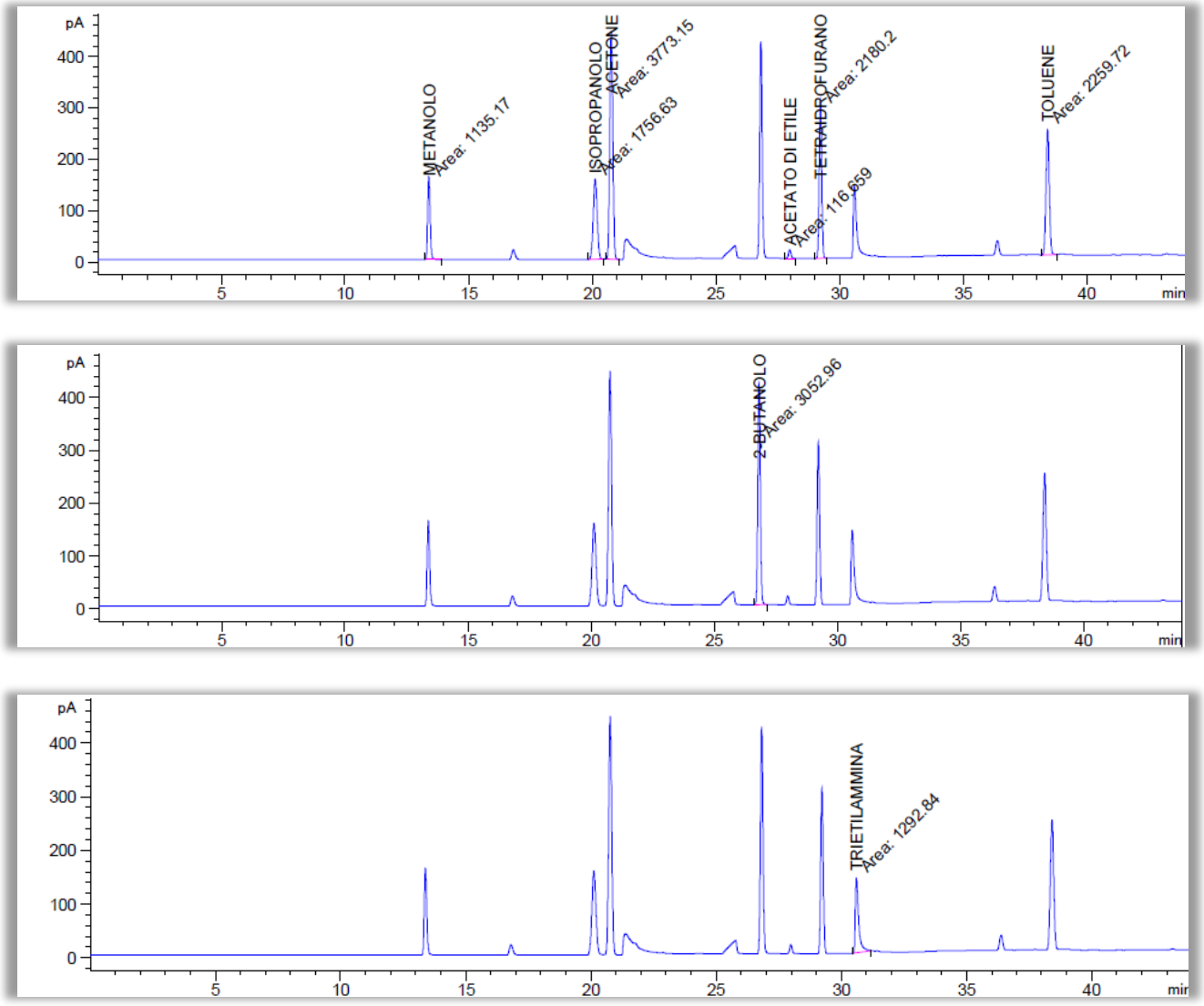



Figure 18: Chromatograms of a waste solvent with the presence of triethylamine

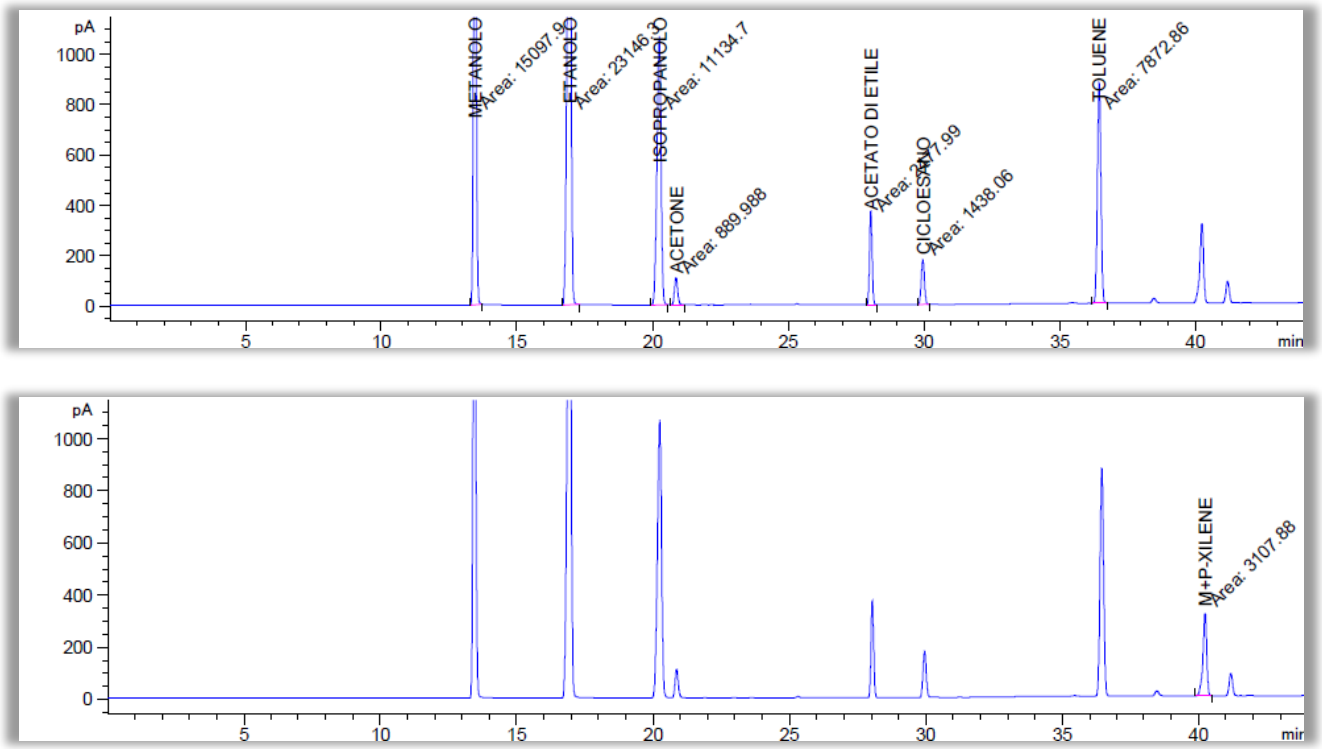



Figure 19: Chromatograms of a waste solvent with the presence of m-xylene and p-xylene

The statistical approach described in this work could be considered as an additional quality assurance used with method EPA 8015D. The development of this method with all the statistical determinations was important to assure a good quality of analytical data. The statistical approach of this study allowed to the analysts to have a good control of the response of the analysis in term of precision and accuracy for all the analytes. The wastes are very complex matrices and the evaluation of recovery is fundamental for the correct expression of the analytical data.

In this work the statistical approach gave the opportunity to understand possible differences between the analytes: each compound was monitored for a long period of time and the results of recovery obtained from ICV, elaborated with ANOVA test, confirmed that all the analytes can be classified in three groups to explain the total variance. This approach is necessary to demonstrate the validity of the analysis carried out in short time and without any pre-treatment of the samples.

## APPENDIX

### A1. Calibration curves

| MEYHANOL | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1510 | 99.03934 |
| 6040 | 618.08781 |
| 15100 | 1998.02847 |
| 22650 | 3066.503989 |
| 30200 | 4356.41784 |

| ETHANOL | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1469.4 | 199.50518 |
| 5877.6 | 1246.49988 |
| 14694 | 3514.46794 |
| 22041 | 4962.54585 |
| 29388 | 6578.41416 |

| ISOPROPANOL | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1486.6 | 208.57998 |
| 5946.4 | 1237.07032 |
| 14866 | 3899.57394 |
| 22299 | 5514.39092 |
| 29732 | 7648.94753 |

| ACETONE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1472.2 | 217.40515 |
| 5888.8 | 1042.07697 |
| 14722 | 3013.10309 |
| 22083 | 4609.35109 |
| 29444 | 6327.02956 |

| ACETONITRILE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1516.6 | 177.37162 |
| 6066.4 | 1070.01883 |
| 15166 | 3407.85297 |
| 22749 | 5006.57719 |
| 30332 | 7322.4987 |

| METHYL ACETATE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1745.2 | 136.41474 |
| 6980.8 | 724.74055 |
| 17452 | 2267.45021 |
| 26178 | 3207.16904 |
| 34904 | 4686.24589 |

| DICHLOROMETANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 2176 | 75.85747 |
| 8704 | 440.40489 |
| 21760 | 1166.66634 |
| 32640 | 2001.67028 |
| 43520 | 2539.84947 |

| HEXANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1255 | 286.40729 |
| 5020 | 1516.36292 |
| 12550 | 4004.41419 |
| 18825 | 5594.20959 |
| 25100 | 7710.93644 |

| 2-BUTANONE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1280.6 | 235.41515 |
| 5122.4 | 1254.4084 |
| 12806 | 3764.35421 |
| 19209 | 5452.88801 |
| 25612 | 7407.34518 |

| ETHYLACETATE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1758.2 | 289.96897 |
| 7032.8 | 1180.43054 |
| 17582 | 3422.84588 |
| 26373 | 4942.15874 |
| 35164 | 6858.82133 |

| TETRAHYDROFURAN | |
|---|---|
| Conc (mg/L) | Peak Area |
| 931.2 | 156.48483 |
| 3724.8 | 825.24937 |
| 9312 | 2405.4199 |
| 13968 | 3439.60198 |
| 18624 | 4854.69105 |

| CYCLOHEXANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1476.6 | 362.50913 |
| 5906.4 | 1817.3864 |
| 14766 | 4960.7652 |
| 22149 | 7109.79997 |
| 29532 | 9782.00064 |

| ISOPROPILACETATE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1711.8 | 274.20331 |
| 6847.2 | 1428.3141 |
| 17118 | 4050.32477 |
| 25677 | 5936.01996 |
| 34236 | 8100.23507 |

| HEPTANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1345.8 | 354.47705 |
| 5383.2 | 1826.87607 |
| 13458 | 5000.33761 |
| 20187 | 7010.44203 |
| 26916 | 9709.13447 |

| 1,4-DIOXANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 2029.4 | 230 |
| 8117.6 | 1207.94165 |
| 20294 | 3605.09985 |
| 30441 | 5071.2391 |
| 40588 | 7097.3501 |

| CYCLO PENTYL METHYL ETHER | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1694.4 | 375.10716 |
| 6777.6 | 2079.13783 |
| 16944 | 5884.1299 |
| 25416 | 8249.42954 |
| 33888 | 11303.8 |

| TOLUENE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1703.6 | 595.74809 |
| 6814.4 | 3073.9899 |
| 17036 | 8874.49762 |
| 25554 | 12368.4 |
| 34072 | 17087.2 |

| BUTHYL ACETATE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1740.2 | 356.02305 |
| 6960.8 | 1939.76129 |
| 17402 | 5478.71433 |
| 26103 | 7606.73477 |
| 34804 | 10467 |

| DIMETHYLFORMAMIDE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1929 | 222.49948 |
| 7716 | 1236.31026 |
| 19290 | 3345.94849 |
| 28935 | 4856.46435 |
| 38580 | 6831.08788 |

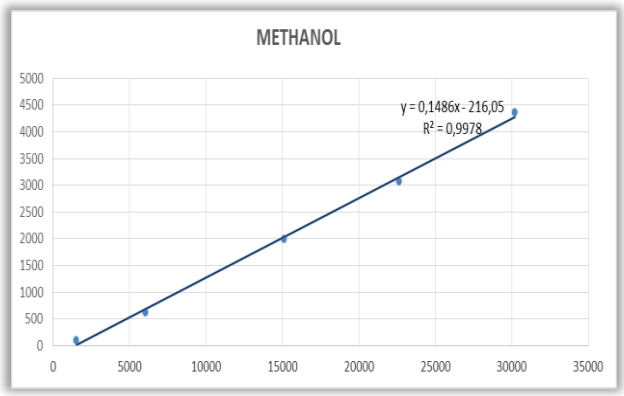
| 2-BUTANOL | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1543.6 | 253.5717 |
| 6174.4 | 1391.18762 |
| 15436 | 3701.89966 |
| 23154 | 6020.95752 |
| 30872 | 8236.18945 |

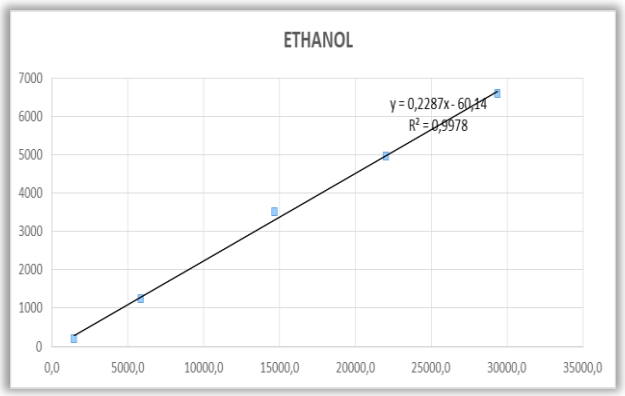
| 1-BUTANOL | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1567.2 | 287.90253 |
| 6268.8 | 1603.1842 |
| 15672 | 4275.42432 |
| 23508 | 6886.77393 |
| 31344 | 9402.22461 |

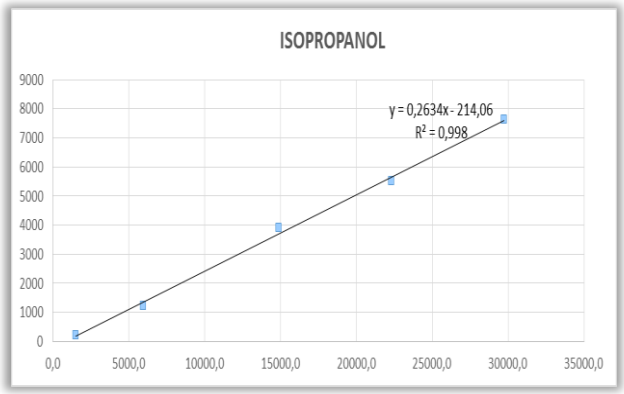
| PYRIDINE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1943.8 | 455.33185 |
| 7775.2 | 2446.01127 |
| 19438 | 6220.23998 |
| 29157 | 10023.2 |
| 38876 | 13601.7 |

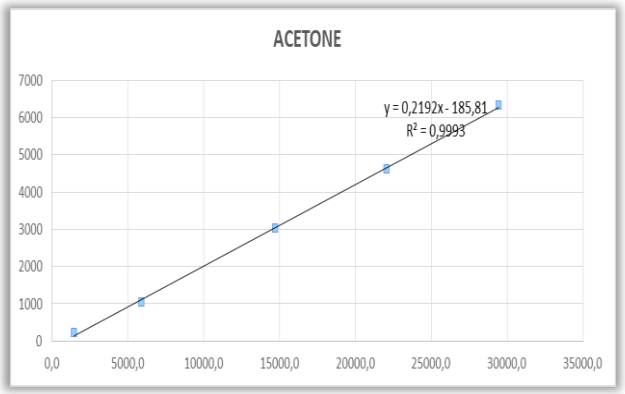
| DIISOPROPYL ETHER | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1382.4 | 268.33295 |
| 5529.6 | 1349.2771 |
| 13824 | 3410.05542 |
| 20736 | 5264.50098 |
| 27648 | 6731.11377 |

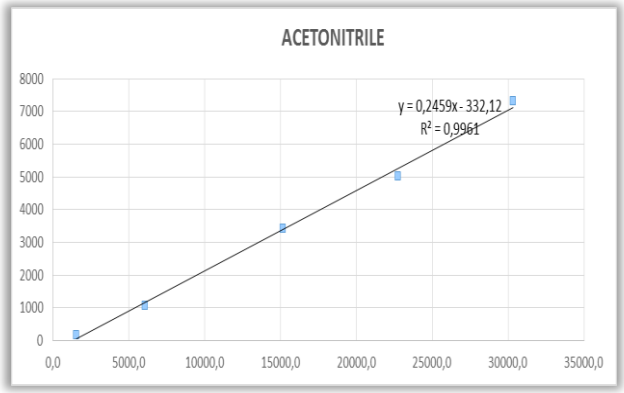
| OCTANE | |
|---|---|
| Conc (mg/L) | Peak Area |
| 1392 | 439.51883 |
| 5568 | 2163.5874 |
| 13920 | 5476.95166 |
| 20880 | 8418.46094 |
| 27840 | 10954.2 |

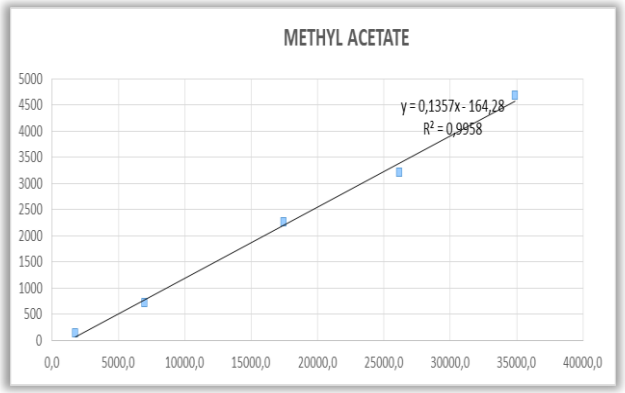

METHANOL
y = 0,1486x - 216,05
R² = 0,9978

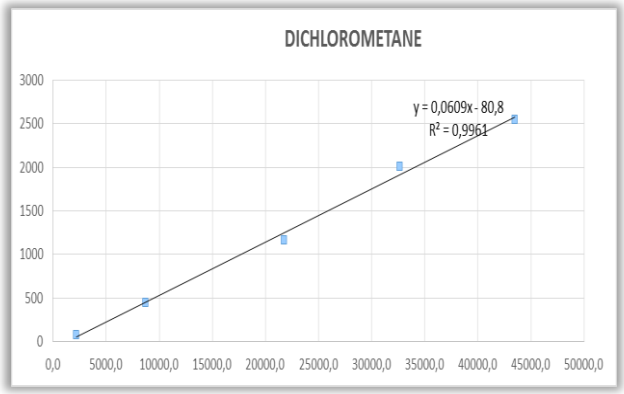

ETHANOL
y = 0,2287x - 60,14
R² = 0,9978

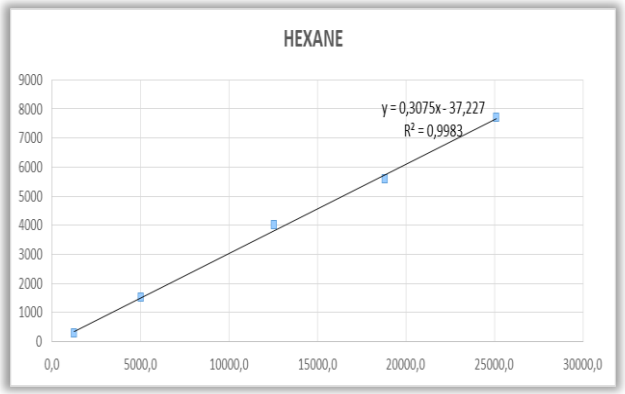

ISOPROPANOL
y = 0,2634x - 214,06
R² = 0,998

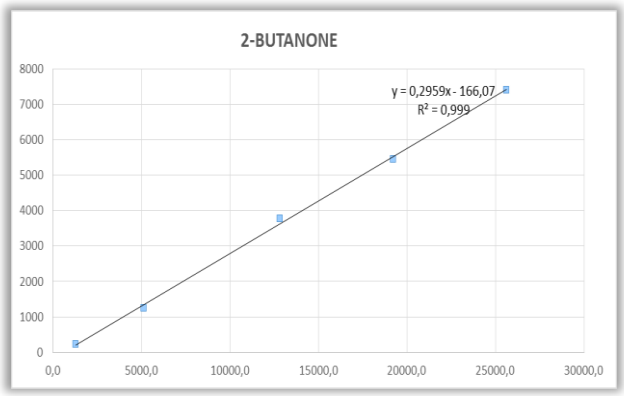

ACETONE
y = 0,2192x - 185,81
R² = 0,9993

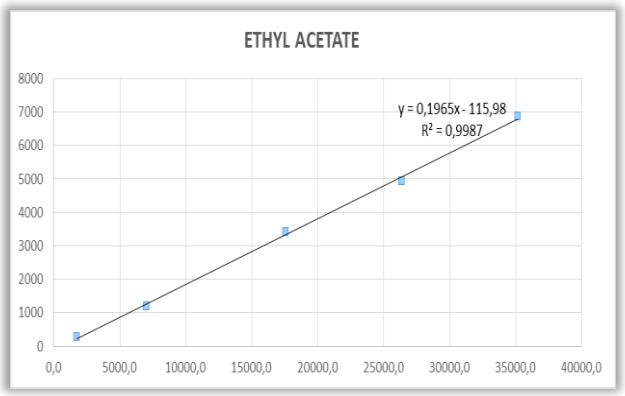

ACETONITRILE
y = 0,2459x - 332,12
R² = 0,9961

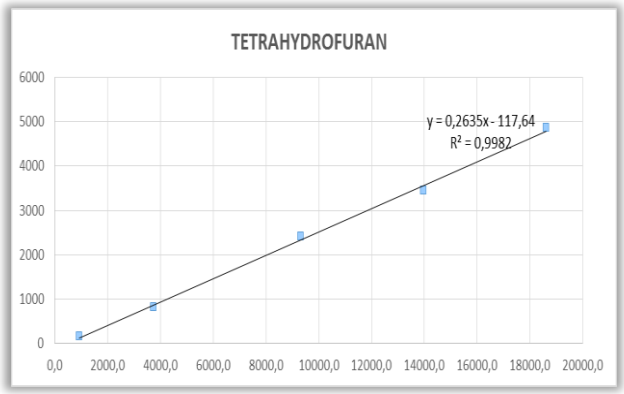

METHYL ACETATE
y = 0,1357x - 164,28
R² = 0,9958

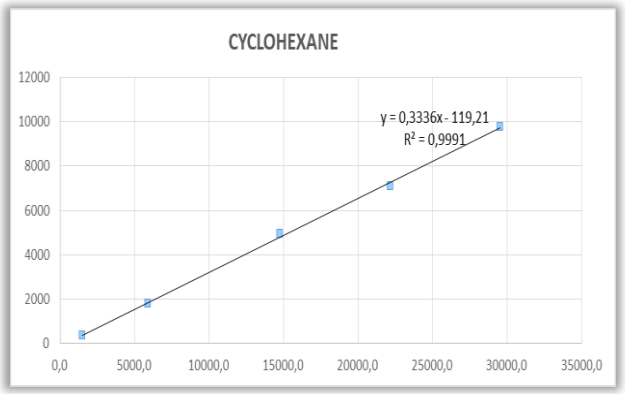

DICHLOROMETANE
y = 0,0609x - 80,8
R² = 0,9961

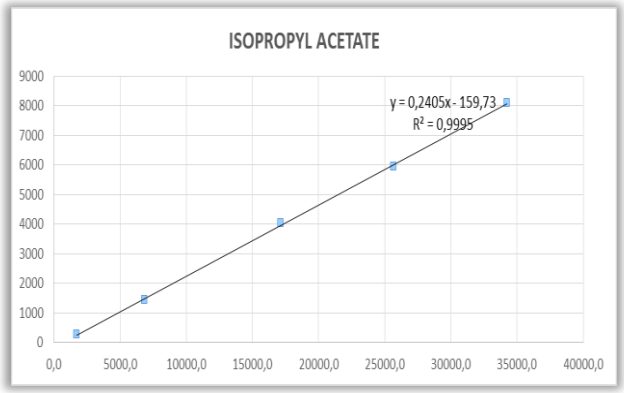

HEXANE
y = 0,3075x - 37,227
R² = 0,9983

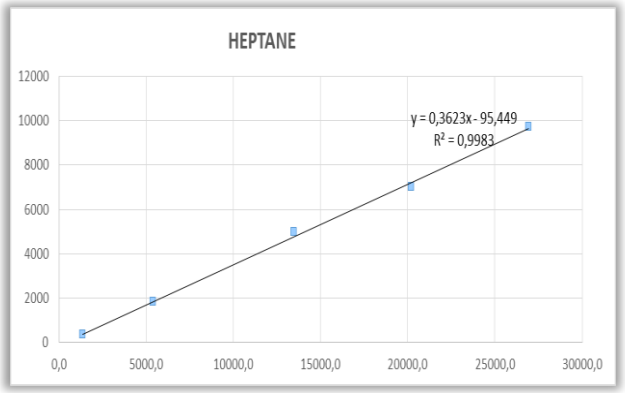

2-BUTANONE
y = 0,2959x - 166,07
R² = 0,999

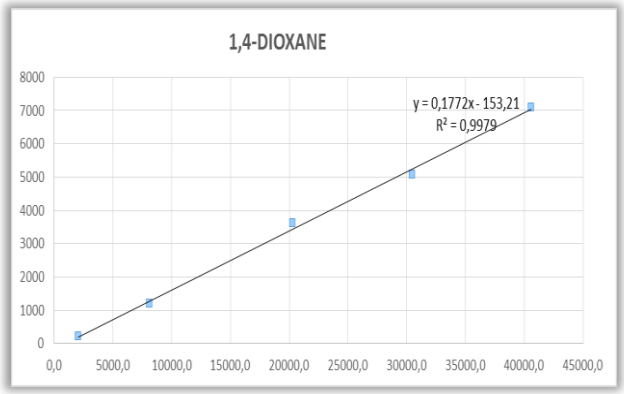

ETHYL ACETATE
y = 0,1965x - 115,98
R² = 0,9987

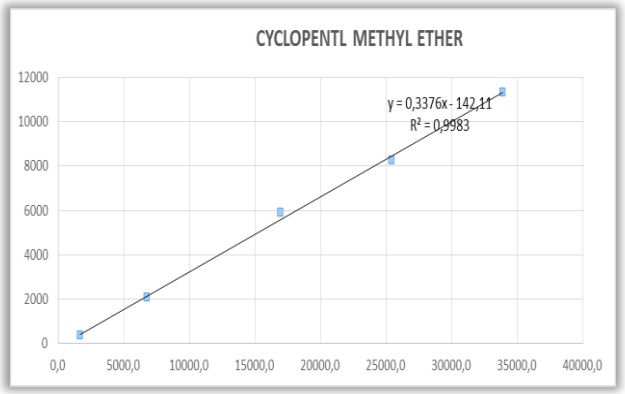

TETRAHYDROFURAN
y = 0,2635x - 117,64
R² = 0,9982

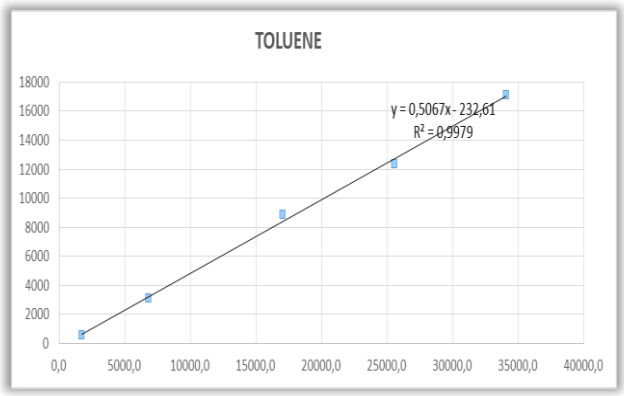

CYCLOHEXANE
y = 0,3336x - 119,21
R² = 0,9991

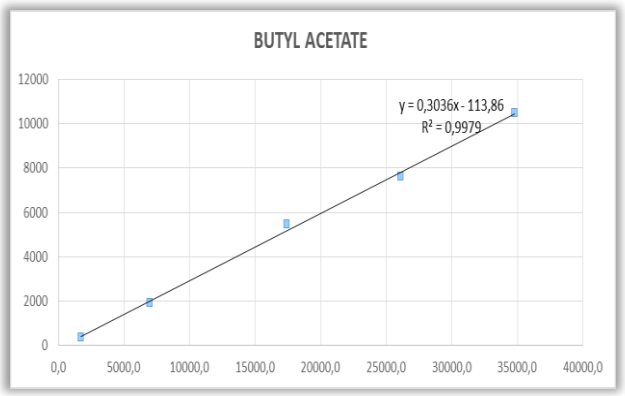

ISOPROPYL ACETATE
y = 0,2405x - 159,73
R² = 0,9995

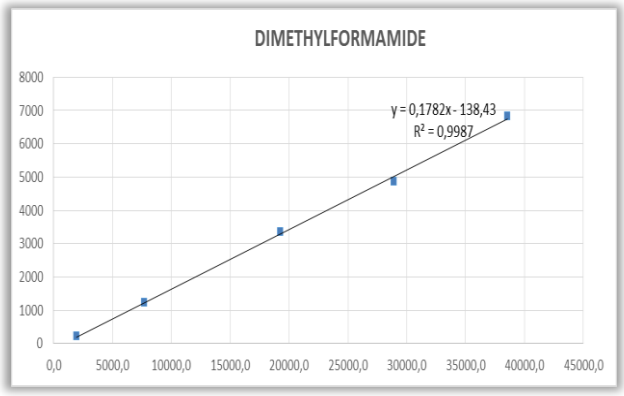

HEPTANE
y = 0,3623x - 95,449
R² = 0,9983

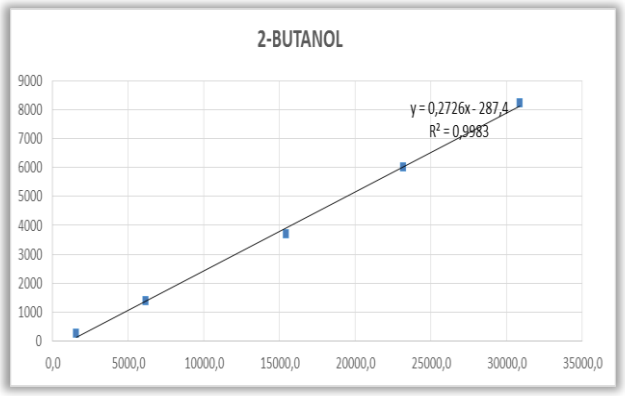

1,4-DIOXANE
y = 0,1772x - 153,21
R² = 0,9979

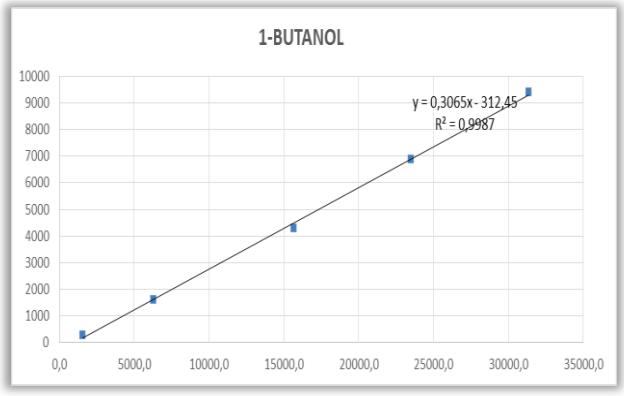

CYCLOPENTL METHYL ETHER
y = 0,3376x - 142,11
R² = 0,9983

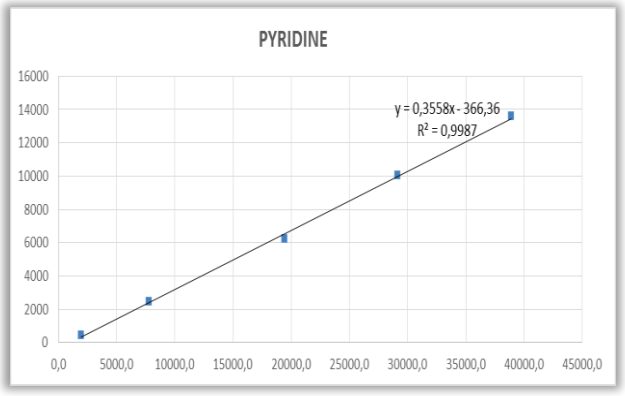

TOLUENE
y = 0,5067x - 232,61
R² = 0,9979

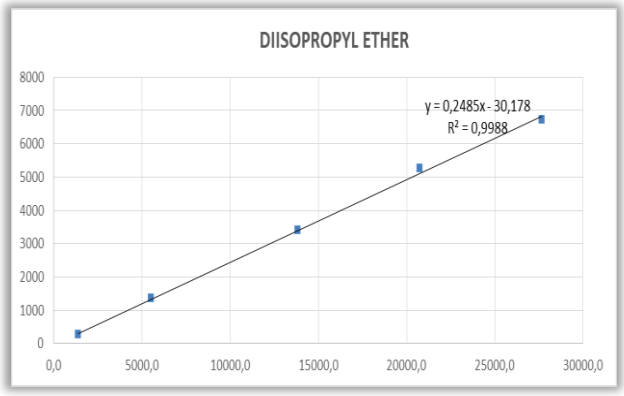

BUTYL ACETATE
y = 0,3036x - 113,86
R² = 0,9979

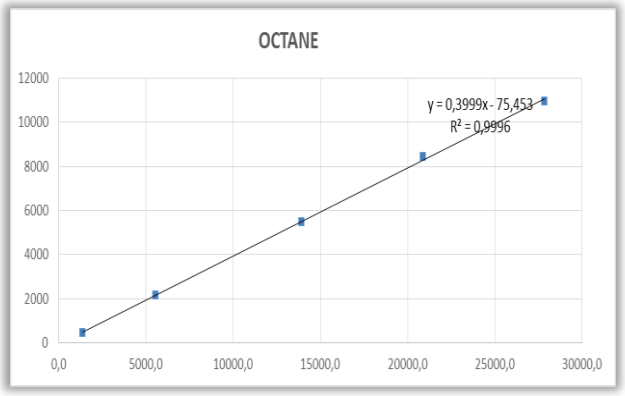

DIMETHYLFORMAMIDE
y = 0,1782x - 138,43
R² = 0,9987


2-BUTANOL
y = 0,2726x - 287,4
R² = 0,9983


1-BUTANOL
y = 0,3065x - 312,45
R² = 0,9987


PYRIDINE
y = 0,3558x - 366,36
R² = 0,9987


DIISOPROPYL ETHER
y = 0,2485x - 30,178
R² = 0,9988


OCTANE
y = 0,3999x - 75,453
R² = 0,9996

## A2. Determination of LOQ and LOD

| METHANOL | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 70.91 |
| 308.00 | 68.80 | 2 | 67.18 |
| 615.00 | 153.72 | 3 | 70.09 |
| 923.00 | 226.10 | 4 | 75.54 |
| 1230.00 | 294.67 | 5 | 70.58 |
| 1538.00 | 389.79 | 6 | 72.61 |
| | | 7 | 71.20 |
| | | 8 | 72.53 |
| Slope | 0.25 | 9 | 76.47 |
| Intercept | -8.34 | 10 | 70.64 |
| LOD mg/L) | 31.72 | STD Dev. | 2.69 |
| LOQ (mg/L) | 105.74 | Mean | 71.78 |

| ETHANOL | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 105.30 |
| 315.00 | 100.03 | 2 | 99.77 |
| 631.00 | 216.25 | 3 | 111.24 |
| 946.00 | 338.93 | 4 | 104.38 |
| 1261.00 | 457.39 | 5 | 107.79 |
| 1576.00 | 572.23 | 6 | 107.69 |
| | | 7 | 109.07 |
| | | 8 | 113.89 |
| Slope | 0.38 | 9 | 108.62 |
| Intercept | -18.77 | 10 | 108.79 |
| LOD mg/L) | 30.82 | STD Dev. | 3.86 |
| LOQ (mg/L) | 102.75 | Mean | 107.65 |

| ISOPROPANOL | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 76.69 |
| 311.00 | 71.05 | 2 | 74.58 |
| 622.00 | 160.94 | 3 | 77.26 |
| 933.00 | 261.32 | 4 | 77.39 |
| 1244.00 | 349.65 | 5 | 78.70 |
| 1555.00 | 473.78 | 6 | 75.51 |
| | | 7 | 81.90 |
| | | 8 | 81.40 |
| Slope | 0.32 | 9 | 76.39 |
| Intercept | -34.90 | 10 | 78.60 |
| LOD mg/L) | 22.23 | STD Dev. | 2.37 |
| LOQ (mg/L) | 74.10 | Mean | 77.84 |

| ACETONITRILE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 111.50 |
| 317.00 | 104.03 | 2 | 103.09 |
| 633.00 | 227.87 | 3 | 119.60 |
| 950.00 | 354.76 | 4 | 110.38 |
| 1266.00 | 482.00 | 5 | 114.14 |
| 1582.00 | 592.22 | 6 | 113.03 |
| | | 7 | 116.94 |
| | | 8 | 120.05 |
| Slope | 0.39 | 9 | 114.90 |
| Intercept | -17.25 | 10 | 114.29 |
| LOD mg/L) | 37.81 | STD Dev. | 4.90 |
| LOQ (mg/L) | 126.04 | Mean | 113.79 |

| METHYL ACETATE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 73.02 |
| 346.00 | 67.33 | 2 | 69.91 |
| 692.00 | 151.84 | 3 | 74.61 |
| 1038.00 | 230.87 | 4 | 70.33 |
| 1384.00 | 298.10 | 5 | 73.61 |
| 1730.00 | 390.41 | 6 | 69.72 |
| | | 7 | 71.73 |
| | | 8 | 75.49 |
| Slope | 0.23 | 9 | 76.67 |
| Intercept | -10.02 | 10 | 72.32 |
| LOD mg/L) | 31.33 | STD Dev. | 2.39 |
| LOQ (mg/L) | 104.42 | Mean | 72.74 |

| DICHLOROMETANE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 53.89 |
| 527.00 | 50.31 | 2 | 50.57 |
| 1054.00 | 109.05 | 3 | 54.64 |
| 1581.00 | 168.24 | 4 | 50.66 |
| 2108.00 | 218.93 | 5 | 53.73 |
| 2635.00 | 273.93 | 6 | 55.32 |
| | | 7 | 53.73 |
| | | 8 | 54.13 |
| Slope | 0.11 | 9 | 50.55 |
| Intercept | -3.04 | 10 | 51.64 |
| LOD mg/L) | 52.08 | STD Dev. | 1.84 |
| LOQ (mg/L) | 173.59 | Mean | 52.89 |

| HEXANE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 148.18 |
| 260.00 | 152.29 | 2 | 135.50 |
| 519.00 | 334.10 | 3 | 148.88 |
| 779.00 | 534.61 | 4 | 141.19 |
| 1038.00 | 661.19 | 5 | 145.31 |
| 1298.00 | 874.54 | 6 | 141.90 |
| | | 7 | 152.19 |
| | | 8 | 153.03 |
| Slope | 0.68 | 9 | 130.42 |
| Intercept | -20.35 | 10 | 146.93 |
| LOD mg/L) | 31.68 | STD Dev. | 7.21 |
| LOQ (mg/L) | 105.62 | Mean | 144.35 |

| 2-BUTANONE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 150.43 |
| 327.00 | 137.24 | 2 | 141.49 |
| 654.00 | 291.66 | 3 | 155.08 |
| 982.00 | 448.64 | 4 | 147.15 |
| 1309.00 | 588.27 | 5 | 150.07 |
| 1637.00 | 775.89 | 6 | 146.09 |
| | | 7 | 148.90 |
| | | 8 | 156.04 |
| Slope | 0.48 | 9 | 155.96 |
| Intercept | -23.50 | 10 | 147.99 |
| LOD mg/L) | 29.35 | STD Dev. | 4.70 |
| LOQ (mg/L) | 97.85 | Mean | 149.92 |

| ETHYL ACETATE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 107.69 |
| 360.00 | 99.85 | 2 | 104.90 |
| 721.00 | 222.33 | 3 | 110.14 |
| 1081.00 | 347.98 | 4 | 109.46 |
| 1441.00 | 441.51 | 5 | 109.44 |
| 1802.00 | 583.67 | 6 | 112.41 |
| | | 7 | 108.16 |
| | | 8 | 116.58 |
| Slope | 0.33 | 9 | 107.84 |
| Intercept | -16.92 | 10 | 105.73 |
| LOD mg/L) | 30.59 | STD Dev. | 3.36 |
| LOQ (mg/L) | 101.98 | Mean | 109.24 |

| TETRAHYDROFURAN | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 119.69 |
| 345.00 | 107.83 | 2 | 114.81 |
| 691.00 | 251.82 | 3 | 123.06 |
| 1036.00 | 400.42 | 4 | 114.87 |
| 1382.00 | 528.20 | 5 | 119.94 |
| 1727.00 | 678.40 | 6 | 127.09 |
| | | 7 | 125.27 |
| | | 8 | 124.64 |
| Slope | 0.41 | 9 | 120.90 |
| Intercept | -31.80 | 10 | 120.08 |
| LOD mg/L) | 30.09 | STD Dev. | 4.11 |
| LOQ (mg/L) | 100.30 | Mean | 121.04 |

| CYCLOHEXANE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 137.49 |
| 302.00 | 137.65 | 2 | 131.40 |
| 603.00 | 312.17 | 3 | 145.79 |
| 905.00 | 513.74 | 4 | 139.83 |
| 1206.00 | 681.15 | 5 | 136.04 |
| 1508.00 | 850.36 | 6 | 148.53 |
| | | 7 | 139.96 |
| | | 8 | 149.01 |
| Slope | 0.60 | 9 | 141.75 |
| Intercept | -39.49 | 10 | 138.52 |
| LOD mg/L) | 28.20 | STD Dev. | 5.60 |
| LOQ (mg/L) | 94.01 | Mean | 140.83 |

| ISOPROPYL ACETATE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 131.23 |
| 352.00 | 128.87 | 2 | 130.66 |
| 703.00 | 287.91 | 3 | 147.38 |
| 1055.00 | 480.45 | 4 | 137.36 |
| 1406.00 | 578.60 | 5 | 141.39 |
| 1758.00 | 730.32 | 6 | 147.07 |
| | | 7 | 153.62 |
| | | 8 | 148.25 |
| Slope | 0.42 | 9 | 114.27 |
| Intercept | -6.98 | 10 | 130.82 |
| LOD mg/L) | 83.04 | STD Dev. | 11.76 |
| LOQ (mg/L) | 276.81 | Mean | 138.21 |

| HEPTANE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 162.17 |
| 267.00 | 155.24 | 2 | 159.97 |
| 533.00 | 316.43 | 3 | 167.07 |
| 800.00 | 490.62 | 4 | 156.07 |
| 1067.00 | 704.10 | 5 | 163.35 |
| 1333.00 | 806.27 | 6 | 166.76 |
| | | 7 | 168.56 |
| | | 8 | 172.30 |
| Slope | 0.63 | 9 | 183.43 |
| Intercept | -12.54 | 10 | 157.99 |
| LOD mg/L) | 37.73 | STD Dev. | 7.97 |
| LOQ (mg/L) | 125.78 | Mean | 165.77 |

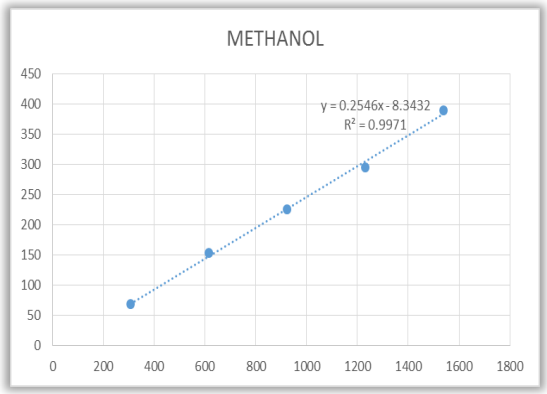
| 1,4-DIOXANE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 138.54 |
| 403.00 | 124.56 | 2 | 123.91 |
| 805.00 | 278.39 | 3 | 144.56 |
| 1208.00 | 436.52 | 4 | 142.38 |
| 1611.00 | 590.21 | 5 | 141.43 |
| 2013.00 | 767.30 | 6 | 141.81 |
| | | 7 | 145.89 |
| | | 8 | 147.45 |
| Slope | 0.40 | 9 | 144.87 |
| Intercept | -39.87 | 10 | 141.11 |
| LOD mg/L) | 50.01 | STD Dev. | 6.61 |
| LOQ (mg/L) | 166.70 | Mean | 141.20 |

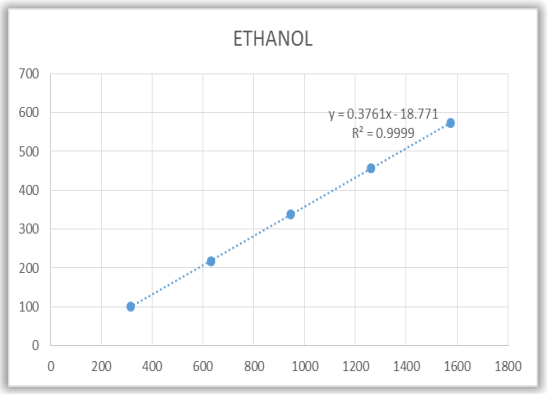
| CYCLOPENTYL METHYL ETHER | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 192.48 |
| 344.00 | 174.15 | 2 | 185.25 |
| 688.00 | 389.42 | 3 | 192.43 |
| 1032.00 | 591.06 | 4 | 186.48 |
| 1376.00 | 787.24 | 5 | 196.46 |
| 1720.00 | 1019.51 | 6 | 197.48 |
| | | 7 | 199.67 |
| | | 8 | 204.08 |
| Slope | 0.61 | 9 | 192.73 |
| Intercept | -34.29 | 10 | 194.24 |
| LOD mg/L) | 28.11 | STD Dev. | 5.69 |
| LOQ (mg/L) | 93.71 | Mean | 194.13 |

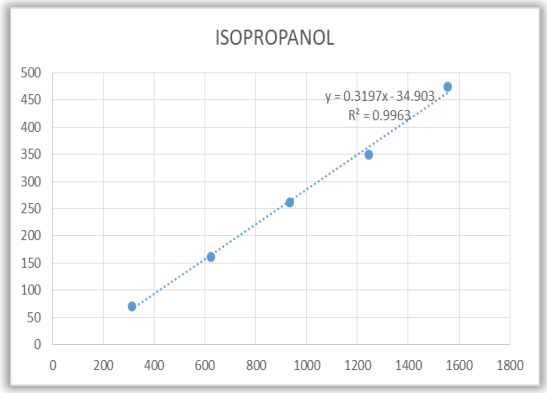
| TOLUENE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 286.16 |
| 347.00 | 266.91 | 2 | 275.64 |
| 694.00 | 575.12 | 3 | 306.88 |
| 1041.00 | 868.07 | 4 | 291.01 |
| 1388.00 | 1181.92 | 5 | 295.13 |
| 1735.00 | 1480.14 | 6 | 297.70 |
| | | 7 | 299.48 |
| | | 8 | 308.61 |
| Slope | 0.87 | 9 | 292.13 |
| Intercept | -35.55 | 10 | 295.62 |
| LOD mg/L) | 32.98 | STD Dev. | 9.61 |
| LOQ (mg/L) | 109.92 | Mean | 294.84 |

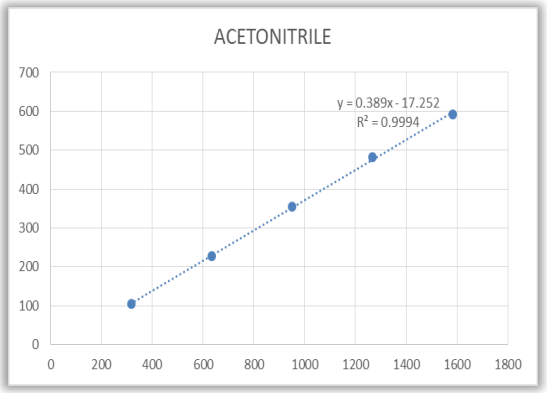
| BUTYL ACETATE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 151.11 |
| 354.00 | 140.79 | 2 | 147.13 |
| 707.00 | 308.47 | 3 | 164.54 |
| 1061.00 | 482.35 | 4 | 152.52 |
| 1415.00 | 651.87 | 5 | 157.12 |
| 1769.00 | 805.73 | 6 | 160.82 |
| | | 7 | 165.54 |
| | | 8 | 159.65 |
| Slope | 0.47 | 9 | 158.25 |
| Intercept | -24.05 | 10 | 151.11 |
| LOD mg/L) | 38.95 | STD Dev. | 6.14 |
| LOQ (mg/L) | 129.84 | Mean | 156.78 |

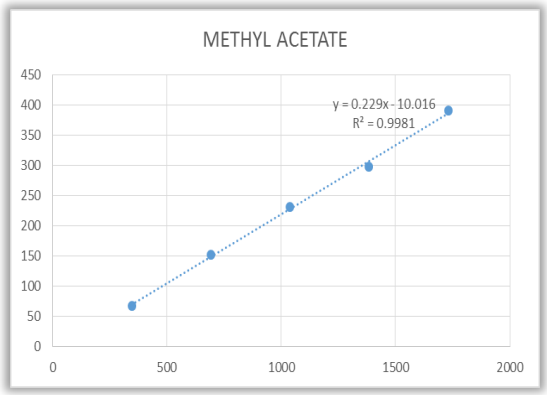
| DIMETHYLFORMAMIDE | | n. | Peak Area |
|---|---|---|---|
| Conc (mg/L) | Peak Area | 1 | 77.83 |
| 347.00 | 71.77 | 2 | 80.50 |
| 695.00 | 161.35 | 3 | 86.39 |
| 1042.00 | 249.40 | 4 | 79.93 |
| 1390.00 | 347.04 | 5 | 82.93 |
| 1737.00 | 439.59 | 6 | 84.92 |
| | | 7 | 88.53 |
| | | 8 | 82.23 |
| Slope | 0.27 | 9 | 83.77 |
| Intercept | -22.49 | 10 | 83.77 |
| LOD mg/L) | 35.76 | STD Dev. | 3.16 |
| LOQ (mg/L) | 119.19 | Mean | 83.08 |

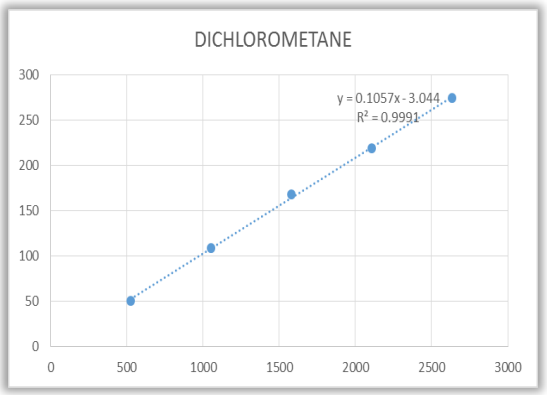

METHANOL
y = 0.2546x - 8.3432
R² = 0.9971

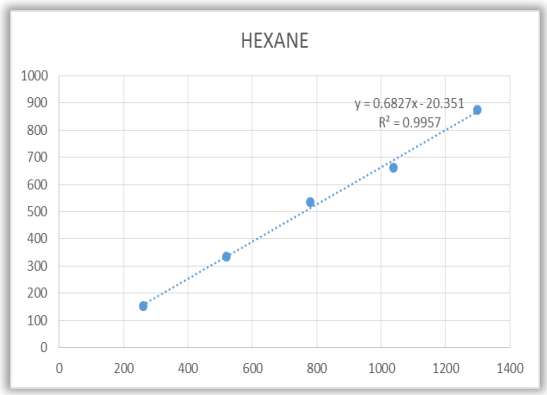

ETHANOL
y = 0.3761x - 18.771
R² = 0.9999

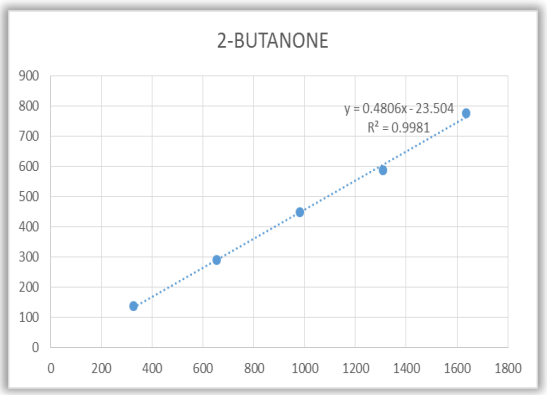

ISOPROPANOL
y = 0.3197x - 34.903
R² = 0.9963

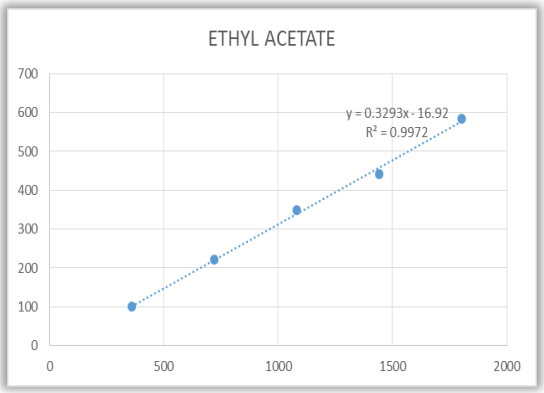

ACETONITRILE
y = 0.389x - 17.252
R² = 0.9994

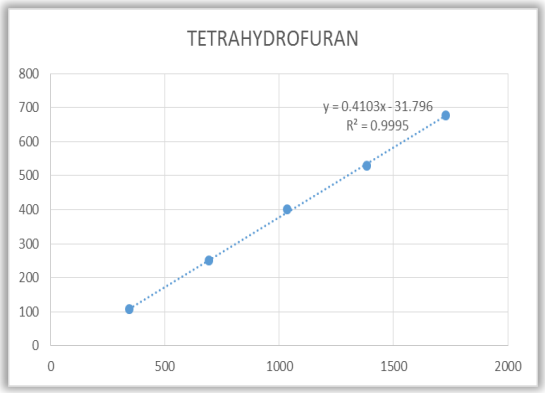

METHYL ACETATE
y = 0.229x - 10.016
R² = 0.9981

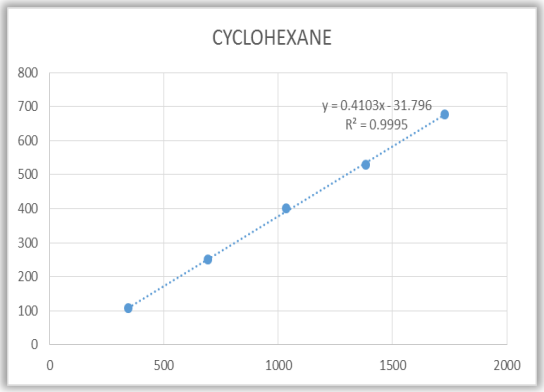

DICHLOROMETANE
y = 0.1057x - 3.044
R² = 0.9991

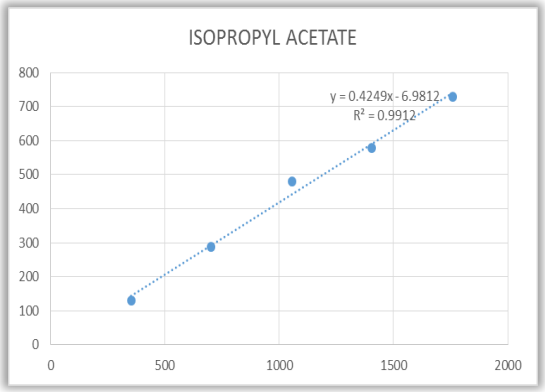

HEXANE
y = 0.6827x - 20.351
R² = 0.9957

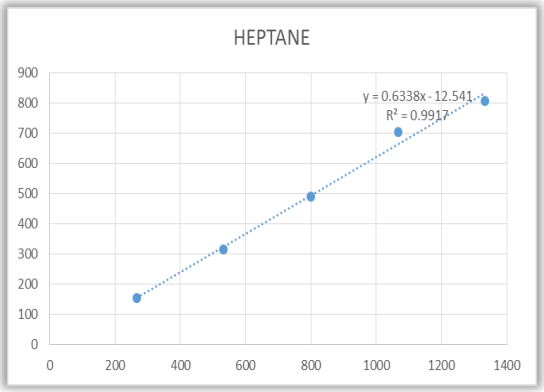

2-BUTANONE
y = 0.4806x - 23.504
R² = 0.9981

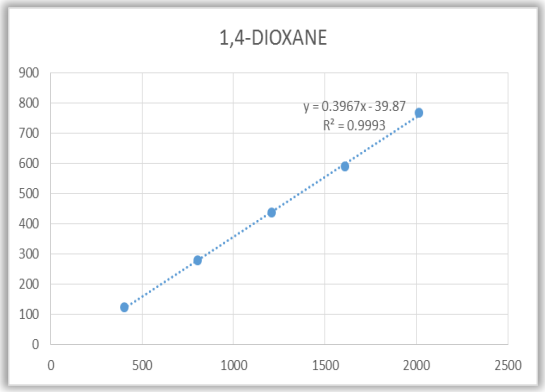

ETHYL ACETATE
y = 0.3293x - 16.92
R² = 0.9972

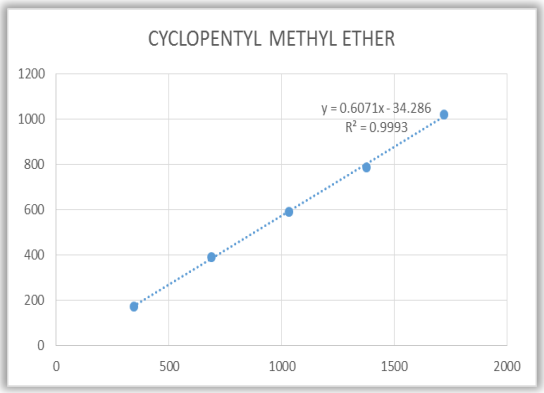

TETRAHYDROFURAN
y = 0.4103x - 31.796
R² = 0.9995

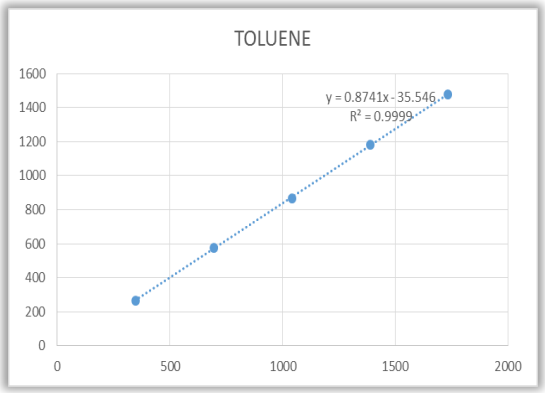

CYCLOHEXANE
y = 0.4103x - 31.796
R² = 0.9995

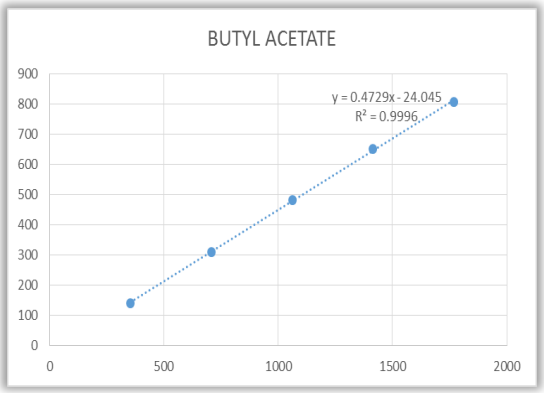

ISOPROPYL ACETATE
y = 0.4249x - 6.9812
R² = 0.9912

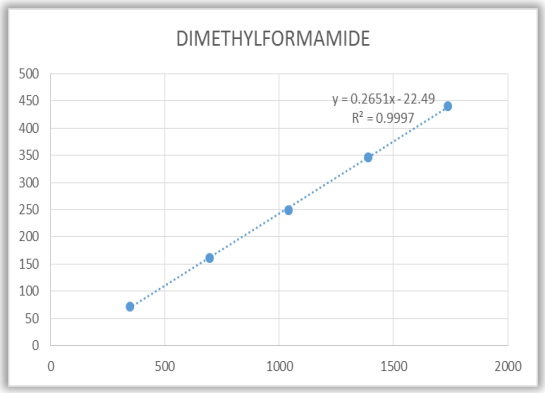

HEPTANE
y = 0.6338x - 12.541
R² = 0.9917


1,4-DIOXANE
y = 0.3967x - 39.87
R² = 0.9993


CYCLOPENTYL METHYL ETHER
y = 0.6071x - 34.286
R² = 0.9993


TOLUENE
y = 0.8741x - 35.546
R² = 0.9999


BUTYL ACETATE
y = 0.4729x - 24.045
R² = 0.9996
900
800
700
600
500
400
300
200
100
0
0
500
1000
1500
2000


DIMETHYLFORMAMIDE
y = 0.2651x - 22.49
R² = 0.9997
500
450
400
350
300
250
200
150
100
50
0
0
500
1000
1500
2000

**A3. Experiments of repeatability on Certified Matrix**

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **METHANOL** | **METHANOL** | **METHANOL** |
| **1** | 2843.04 | 10644.30 | 13592.41 |
| **2** | 2850.63 | 10651.90 | 14039.24 |
| **3** | 2931.65 | 10713.92 | 14050.63 |
| **4** | 2953.16 | 11353.16 | 14882.28 |
| **5** | 2954.43 | 12007.59 | 15454.43 |
| **6** | 2982.28 | 12192.41 | 15726.58 |
| **7** | 3012.66 | 12294.94 | 16467.09 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2531.65 | 12658.23 | 16911.39 |

| | | | |
|---|---|---|---|
| **Mean** | 2932.55 | 11408.32 | 14887.52 |
| **STD Dev.** | 63.92 | 752.90 | 1050.22 |
| **CV%** | 2.18 | 6.60 | 7.05 |
| **Variance** | 4086.27 | 566855.13 | 1102959.69 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **METHANOL** | **METHANOL** | **METHANOL** |
| **1** | 112.30 | 84.09 | 80.37 |
| **2** | 112.60 | 84.15 | 83.02 |
| **3** | 115.80 | 84.64 | 83.08 |
| **4** | 116.65 | 89.69 | 88.00 |
| **5** | 116.70 | 94.86 | 91.38 |
| **6** | 117.80 | 96.32 | 92.99 |
| **7** | 119.00 | 97.13 | 97.37 |

| | | | |
|---|---|---|---|
| **Mean** | 115.84 | 90.13 | 88.03 |
| **STD Dev.** | 2.52 | 5.95 | 6.21 |
| **CV%** | 0.02 | 0.07 | 0.07 |
| **Variance** | 6.38 | 35.38 | 38.57 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **METHANOL** | **METHANOL** | **METHANOL** |
| **1** | -1.40 | -1.01 | -1.23 |
| **2** | -1.28 | -1.00 | -0.81 |
| **3** | -0.01 | -0.92 | -0.80 |
| **4** | 0.32 | -0.07 | 0.00 |
| **5** | 0.34 | 0.80 | 0.54 |
| **6** | 0.78 | 1.04 | 0.80 |
| **7** | 1.25 | 1.18 | 1.50 |

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHANOL** | **ETHANOL** | **ETHANOL** |
| **1** | 2664.13 | 11581.75 | 15007.60 |
| **2** | 2737.64 | 11676.81 | 15330.80 |
| **3** | 2792.14 | 11787.07 | 15338.40 |
| **4** | 2795.94 | 12515.84 | 15889.73 |
| **5** | 2826.36 | 13604.56 | 16342.21 |
| **6** | 2830.16 | 13918.88 | 16877.06 |
| **7** | 3095.06 | 13959.44 | 17794.68 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2534.85 | 12674.27 | 16932.83 |

| | | | |
|---|---|---|---|
| **Mean** | 2820.21 | 12720.62 | 16082.93 |
| **STD Dev.** | 134.31 | 1084.12 | 995.12 |
| **CV%** | 4.76 | 8.52 | 6.19 |
| **Variance** | 18038.71 | 1175315.56 | 990269.06 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHANOL** | **ETHANOL** | **ETHANOL** |
| **1** | 105.10 | 91.38 | 88.63 |
| **2** | 108.00 | 92.13 | 90.54 |
| **3** | 110.15 | 93.00 | 90.58 |
| **4** | 110.30 | 98.75 | 93.84 |
| **5** | 111.50 | 107.34 | 96.51 |
| **6** | 111.65 | 109.82 | 99.67 |
| **7** | 122.10 | 110.14 | 105.09 |

| | | | |
|---|---|---|---|
| **Mean** | 111.26 | 100.37 | 94.98 |
| **STD Dev.** | 5.30 | 8.55 | 5.88 |
| **CV%** | 0.05 | 0.09 | 0.06 |
| **Variance** | 28.07 | 73.17 | 34.54 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHANOL** | **ETHANOL** | **ETHANOL** |
| **1** | -1.16 | -1.05 | -1.08 |
| **2** | -0.61 | -0.96 | -0.76 |
| **3** | -0.21 | -0.86 | -0.75 |
| **4** | -0.18 | -0.19 | -0.19 |
| **5** | 0.05 | 0.82 | 0.26 |
| **6** | 0.07 | 1.11 | 0.80 |
| **7** | 2.05 | 1.14 | 1.72 |

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ISOPROPANOL** | **ISOPROPANOL** | **ISOPROPANOL** |
| **1** | 2553.44 | 10527.99 | 13016.54 |
| **2** | 2601.78 | 10568.70 | 13998.73 |
| **3** | 2622.14 | 10623.41 | 14108.14 |
| **4** | 2661.58 | 11793.89 | 14891.86 |
| **5** | 2669.21 | 12075.06 | 15226.46 |
| **6** | 2723.92 | 12248.09 | 15863.87 |
| **7** | 3017.81 | 12363.87 | 16138.68 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2544.53 | 12722.65 | 16997.46 |

| | | | |
|---|---|---|---|
| **Mean** | 2692.84 | 11457.29 | 14749.18 |
| **STD Dev.** | 153.21 | 845.65 | 1110.37 |
| **CV%** | 5.69 | 7.38 | 7.53 |
| **Variance** | 23472.07 | 715123.25 | 1232922.86 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ISOPROPANOL** | **ISOPROPANOL** | **ISOPROPANOL** |
| **1** | 100.35 | 82.75 | 76.58 |
| **2** | 102.25 | 83.07 | 82.36 |
| **3** | 103.05 | 83.50 | 83.00 |
| **4** | 104.60 | 92.70 | 87.61 |
| **5** | 104.90 | 94.91 | 89.58 |
| **6** | 107.05 | 96.27 | 93.33 |
| **7** | 118.60 | 97.18 | 94.95 |

| | | | |
|---|---|---|---|
| **Mean** | 105.83 | 90.05 | 86.77 |
| **STD Dev.** | 6.02 | 6.65 | 6.53 |
| **CV%** | 0.06 | 0.07 | 0.08 |
| **Variance** | 36.25 | 44.18 | 42.67 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ISOPROPANOL** | **ISOPROPANOL** | **ISOPROPANOL** |
| **1** | -0.91 | -1.10 | -1.56 |
| **2** | -0.59 | -1.05 | -0.68 |
| **3** | -0.46 | -0.99 | -0.58 |
| **4** | -0.20 | 0.40 | 0.13 |
| **5** | -0.15 | 0.73 | 0.43 |
| **6** | 0.20 | 0.94 | 1.00 |
| **7** | 2.12 | 1.07 | 1.25 |

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ACETONITRILE** | **ACETONITRILE** | **ACETONITRILE** |
| **1** | 2896.95 | 9936.39 | 12435.11 |
| **2** | 2907.12 | 9963.10 | 13160.31 |
| **3** | 2912.21 | 10792.62 | 14217.56 |
| **4** | 3008.91 | 10792.62 | 14718.83 |
| **5** | 3012.72 | 11016.54 | 14743.00 |
| **6** | 3041.98 | 11134.86 | 14936.39 |
| **7** | 3260.81 | 11215.01 | 15468.19 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2544.53 | 12722.65 | 16997.46 |

| | | | |
|---|---|---|---|
| **Mean** | 3005.82 | 10693.02 | 14239.91 |
| **STD Dev.** | 126.98 | 531.90 | 1072.35 |
| **CV%** | 4.22 | 4.97 | 7.53 |
| **Variance** | 16123.91 | 282912.54 | 1149926.44 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ACETONITRILE** | **ACETONITRILE** | **ACETONITRILE** |
| **1** | 113.85 | 78.10 | 73.16 |
| **2** | 114.25 | 78.31 | 77.43 |
| **3** | 114.45 | 84.83 | 83.65 |
| **4** | 118.25 | 84.83 | 86.59 |
| **5** | 118.40 | 86.59 | 86.74 |
| **6** | 119.55 | 87.52 | 87.87 |
| **7** | 128.15 | 88.15 | 91.00 |

| | | | |
|---|---|---|---|
| **Mean** | 118.13 | 84.05 | 83.78 |
| **STD Dev.** | 4.99 | 4.18 | 6.31 |
| **CV%** | 0.04 | 0.05 | 0.08 |
| **Variance** | 24.90 | 17.48 | 39.80 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ACETONITRILE** | **ACETONITRILE** | **ACETONITRILE** |
| **1** | -0.86 | -1.42 | -1.68 |
| **2** | -0.78 | -1.37 | -1.01 |
| **3** | -0.74 | 0.19 | -0.02 |
| **4** | 0.02 | 0.19 | 0.45 |
| **5** | 0.05 | 0.61 | 0.47 |
| **6** | 0.28 | 0.83 | 0.65 |
| **7** | 2.01 | 0.98 | 1.15 |

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHYL ACETATE** | **ETHYL ACETATE** | **ETHYL ACETATE** |
| **1** | 2008.92 | 9516.16 | 11885.17 |
| **2** | 2023.41 | 9560.76 | 12598.66 |
| **3** | 2088.07 | 9626.53 | 12897.44 |
| **4** | 2100.33 | 10711.26 | 13554.07 |
| **5** | 2115.94 | 11212.93 | 14033.44 |
| **6** | 2127.09 | 11241.92 | 14060.20 |
| **7** | 2265.22 | 11350.06 | 14842.81 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2229.65 | 11148.27 | 15161.65 |

| | | | |
|---|---|---|---|
| **Mean** | 2104.14 | 10459.95 | 13410.26 |
| **STD Dev.** | 84.13 | 859.05 | 1010.88 |
| **CV%** | 4.00 | 8.21 | 7.54 |
| **Variance** | 7078.14 | 737960.03 | 1021871.91 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHYL ACETATE** | **ETHYL ACETATE** | **ETHYL ACETATE** |
| **1** | 90.10 | 85.36 | 78.39 |
| **2** | 90.75 | 85.76 | 83.10 |
| **3** | 93.65 | 86.35 | 85.07 |
| **4** | 94.20 | 96.08 | 89.40 |
| **5** | 94.90 | 100.58 | 92.56 |
| **6** | 95.40 | 100.84 | 92.74 |
| **7** | 101.60 | 101.81 | 97.90 |

| | | | |
|---|---|---|---|
| **Mean** | 94.37 | 93.83 | 88.45 |
| **STD Dev.** | 3.77 | 7.71 | 6.67 |
| **CV%** | 0.04 | 0.08 | 0.08 |
| **Variance** | 14.24 | 59.38 | 44.45 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **ETHYL ACETATE** | **ETHYL ACETATE** | **ETHYL ACETATE** |
| **1** | -1.13 | -1.10 | -1.51 |
| **2** | -0.96 | -1.05 | -0.80 |
| **3** | -0.19 | -0.97 | -0.51 |
| **4** | -0.05 | 0.29 | 0.14 |
| **5** | 0.14 | 0.88 | 0.62 |
| **6** | 0.27 | 0.91 | 0.64 |
| **7** | 1.91 | 1.04 | 1.42 |

| Experimental Data | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **TOLUENE** | **TOLUENE** | **TOLUENE** |
| **1** | 2404.84 | 10309.11 | 13396.77 |
| **2** | 2433.68 | 10831.60 | 14506.34 |
| **3** | 2472.90 | 10900.81 | 14587.08 |
| **4** | 2506.34 | 10982.70 | 15475.20 |
| **5** | 2522.49 | 12298.73 | 15814.30 |
| **6** | 2531.72 | 12805.07 | 15867.36 |
| **7** | 2801.85 | 12848.90 | 16867.36 |

| | | | |
|---|---|---|---|
| **Spike (mg/L)** | 2306.81 | 11534.03 | 15409.46 |

| | | | |
|---|---|---|---|
| **Mean** | 2524.83 | 11568.13 | 15216.35 |
| **STD Dev.** | 130.73 | 1050.38 | 1139.09 |
| **CV%** | 5.18 | 9.08 | 7.49 |
| **Variance** | 17089.04 | 1103306.85 | 1297525.02 |

| Recovery % | Recovery %_Level 1 | Recovery %_Level 2 | Recovery %_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **TOLUENE** | **TOLUENE** | **TOLUENE** |
| **1** | 104.25 | 89.38 | 86.94 |
| **2** | 105.50 | 93.91 | 94.14 |
| **3** | 107.20 | 94.51 | 94.66 |
| **4** | 108.65 | 95.22 | 100.43 |
| **5** | 109.35 | 106.63 | 102.63 |
| **6** | 109.75 | 111.02 | 102.97 |
| **7** | 121.46 | 111.40 | 109.46 |

| | | | |
|---|---|---|---|
| **Mean** | 109.45 | 100.30 | 98.75 |
| **STD Dev.** | 5.67 | 9.11 | 7.39 |
| **CV%** | 0.05 | 0.09 | 0.07 |
| **Variance** | 32.11 | 82.93 | 54.64 |

| Z-SCORE | Conc (mg/L)_Level 1 | Conc (mg/L)_Level 2 | Conc (mg/L)_Level 3 |
|---|---|---|---|
| **EXPERIMENTS** | **TOLUENE** | **TOLUENE** | **TOLUENE** |
| **1** | -0.92 | -1.20 | -1.60 |
| **2** | -0.70 | -0.70 | -0.62 |
| **3** | -0.40 | -0.64 | -0.55 |
| **4** | -0.14 | -0.56 | 0.23 |
| **5** | -0.02 | 0.70 | 0.52 |
| **6** | 0.05 | 1.18 | 0.57 |
| **7** | 2.12 | 1.22 | 1.45 |

## A4. Experimental Data of Recovery % of six target compounds

| RECOVERY % | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| EXPERIMENTS | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| 1 | 116.37 | 108.65 | 99.48 | 111.52 | 114.71 | 109.69 |
| 2 | 99.88 | 122.82 | 100.48 | 97.24 | 101.12 | 97.71 |
| 3 | 111.35 | 130.43 | 111.73 | 108.92 | 113.18 | 109.08 |
| 4 | 112.37 | 93.82 | 113.03 | 109.26 | 113.21 | 107.92 |
| 5 | 109.88 | 117.37 | 109.72 | 107.60 | 108.01 | 105.71 |
| 6 | 109.35 | 114.38 | 112.55 | 107.21 | 111.14 | 106.54 |
| 7 | 119.42 | 114.38 | 112.55 | 118.11 | 111.14 | 118.09 |
| 8 | 111.37 | 112.56 | 113.57 | 110.08 | 114.03 | 112.42 |
| 9 | 117.54 | 101.75 | 114.73 | 117.71 | 120.39 | 120.58 |
| 10 | 105.82 | 96.69 | 107.45 | 104.96 | 106.57 | 105.84 |
| 11 | 96.94 | 96.43 | 100.19 | 97.00 | 98.53 | 98.77 |
| 12 | 104.16 | 102.62 | 108.68 | 104.55 | 105.81 | 105.13 |
| 13 | 105.45 | 107.40 | 109.67 | 105.81 | 106.76 | 104.73 |
| 14 | 116.75 | 113.14 | 119.44 | 116.47 | 116.12 | 110.75 |
| 15 | 120.97 | 125.23 | 123.31 | 120.17 | 119.69 | 113.84 |
| 16 | 118.48 | 121.57 | 121.34 | 118.36 | 115.70 | 109.51 |
| 17 | 102.26 | 109.30 | 107.61 | 104.11 | 104.59 | 102.41 |
| 18 | 107.50 | 117.25 | 112.12 | 109.42 | 104.68 | 94.40 |
| 19 | 117.85 | 119.75 | 117.49 | 113.48 | 115.79 | 119.28 |
| 20 | 113.67 | 117.39 | 122.72 | 116.08 | 115.16 | 109.72 |
| 21 | 112.18 | 120.21 | 113.05 | 101.01 | 111.86 | 109.31 |
| 22 | 106.84 | 109.32 | 108.51 | 96.25 | 106.85 | 103.56 |
| 23 | 113.37 | 120.24 | 115.72 | 103.01 | 113.77 | 112.54 |
| 24 | 111.34 | 116.17 | 114.31 | 101.54 | 111.91 | 110.44 |
| 25 | 115.69 | 115.37 | 119.16 | 105.68 | 115.70 | 113.53 |

| RECOVERY % | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| DIMENSION | 25 | 25 | 25 | 25 | 25 | 25 |
| MEAN | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| STD DEV. | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |

| RECOVERY % | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| Minimum | 96.94 | 93.82 | 99.48 | 96.25 | 98.53 | 94.40 |
| Maximum | 120.97 | 130.43 | 123.31 | 120.17 | 120.39 | 120.58 |
| Sum | 2776.80 | 2824.23 | 2808.59 | 2705.53 | 2776.45 | 2711.49 |
| Points | 25.00 | 25.00 | 25.00 | 25.00 | 25.00 | 25.00 |
| Mean | 111.07 | 112.97 | 112.34 | 108.22 | 111.06 | 108.46 |
| Median | 111.37 | 114.38 | 112.55 | 107.60 | 111.91 | 109.31 |
| RMS | 111.24 | 113.33 | 112.52 | 108.44 | 111.19 | 108.64 |
| StdDeviation | 6.30 | 9.29 | 6.45 | 7.00 | 5.56 | 6.35 |
| Variance | 39.65 | 86.22 | 41.61 | 49.02 | 30.87 | 40.38 |
| StdError | 1.26 | 1.86 | 1.29 | 1.40 | 1.11 | 1.27 |
| Skewness | -0.46 | -0.46 | -0.31 | 0.04 | -0.45 | -0.17 |
| Kurtosis | -0.52 | -0.39 | -0.27 | -0.92 | -0.47 | -0.09 |

## A5. Experimental Data of Recovery % of 24 compounds

| RECOVERY % | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Group 7 | Group 8 |
|---|---|---|---|---|---|---|---|---|
| n. | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHYL ACETATE | DICHLOROMETANE | HEXANE |
| 1 | 100.24 | 104.07 | 98.36 | 102.65 | 99.73 | 100.94 | 105.83 | 125.15 |
| 2 | 84.14 | 88.54 | 84.88 | 88.42 | 84.43 | 88.08 | 92.00 | 111.24 |
| 3 | 91.22 | 95.85 | 91.71 | 95.78 | 91.21 | 94.81 | 99.30 | 118.76 |
| 4 | 95.17 | 99.07 | 94.70 | 99.48 | 94.92 | 98.19 | 103.00 | 118.67 |
| 5 | 94.56 | 97.57 | 93.07 | 98.20 | 93.92 | 95.53 | 100.09 | 108.64 |
| 6 | 99.73 | 110.55 | 96.84 | 103.02 | 98.16 | 101.02 | 105.34 | 110.84 |
| 7 | 95.51 | 106.91 | 93.36 | 98.33 | 94.38 | 96.24 | 100.99 | 102.39 |
| 8 | 97.28 | 109.56 | 94.95 | 100.09 | 95.98 | 97.89 | 103.15 | 105.82 |
| 9 | 98.62 | 112.90 | 96.33 | 102.46 | 98.60 | 99.70 | 103.64 | 99.66 |
| 10 | 103.71 | 108.70 | 101.35 | 107.39 | 103.46 | 104.05 | 108.01 | 100.59 |
| 11 | 100.83 | 104.68 | 98.46 | 104.50 | 100.93 | 101.03 | 104.49 | 91.67 |
| 12 | 104.72 | 107.51 | 102.99 | 108.82 | 105.24 | 104.40 | 108.11 | 96.23 |
| 13 | 105.62 | 108.10 | 102.18 | 109.10 | 105.48 | 102.73 | 108.32 | 89.13 |
| 14 | 105.90 | 121.12 | 104.64 | 109.12 | 106.97 | 104.31 | 107.47 | 83.91 |
| 15 | 102.61 | 115.12 | 94.53 | 103.54 | 98.73 | 105.01 | 105.85 | 138.66 |
| 16 | 86.25 | 89.65 | 81.71 | 87.04 | 84.05 | 88.71 | 89.20 | 113.97 |
| 17 | 100.14 | 101.29 | 93.41 | 101.13 | 96.99 | 101.69 | 102.47 | 126.14 |
| 18 | 89.81 | 102.25 | 85.73 | 89.78 | 87.86 | 90.54 | 90.48 | 107.86 |
| 19 | 85.64 | 90.61 | 83.36 | 86.20 | 84.74 | 87.05 | 86.81 | 100.88 |
| 20 | 90.40 | 91.73 | 87.43 | 90.77 | 89.73 | 91.04 | 91.09 | 100.76 |
| 21 | 90.55 | 92.57 | 87.43 | 91.28 | 89.68 | 90.81 | 90.67 | 97.24 |
| 22 | 91.92 | 95.53 | 90.38 | 92.25 | 92.20 | 92.21 | 91.40 | 93.56 |
| 23 | 92.90 | 96.07 | 90.75 | 92.93 | 93.29 | 92.33 | 92.04 | 90.62 |
| 24 | 99.83 | 96.25 | 96.21 | 101.67 | 99.86 | 102.67 | 102.95 | 126.93 |
| 25 | 100.11 | 104.45 | 98.39 | 100.95 | 100.79 | 101.54 | 101.22 | 118.10 |
| 26 | 86.29 | 82.88 | 83.73 | 87.62 | 86.08 | 88.14 | 88.80 | 109.19 |
| 27 | 102.39 | 95.50 | 97.52 | 103.42 | 101.84 | 103.56 | 103.85 | 122.93 |
| 28 | 102.23 | 98.11 | 98.70 | 103.67 | 102.54 | 103.88 | 103.94 | 118.68 |
| 29 | 86.95 | 84.30 | 86.98 | 87.80 | 88.60 | 87.05 | 86.80 | 87.39 |
| 30 | 92.98 | 99.38 | 96.03 | 92.93 | 96.45 | 91.35 | 90.06 | 78.93 |
| 31 | 101.97 | 98.39 | 101.07 | 101.78 | 104.23 | 102.30 | 101.92 | 99.29 |
| 32 | 95.79 | 89.98 | 91.08 | 97.81 | 95.51 | 97.09 | 97.20 | 111.07 |
| 33 | 102.83 | 96.60 | 99.49 | 103.89 | 103.86 | 102.77 | 102.24 | 105.31 |
| 34 | 104.42 | 97.67 | 99.34 | 106.36 | 104.70 | 108.13 | 109.46 | 141.90 |
| 35 | 100.67 | 96.69 | 98.27 | 101.38 | 102.00 | 101.82 | 102.46 | 118.23 |
| 36 | 97.54 | 95.43 | 97.03 | 98.15 | 99.76 | 98.95 | 98.87 | 107.85 |
| 37 | 95.54 | 95.12 | 97.16 | 96.22 | 99.06 | 96.60 | 96.19 | 99.42 |
| 38 | 96.14 | 95.61 | 98.37 | 95.93 | 99.94 | 95.83 | 94.91 | 91.74 |
| 39 | 89.48 | 85.93 | 86.77 | 89.68 | 90.25 | 90.62 | 91.47 | 106.94 |
| 40 | 94.19 | 92.47 | 93.20 | 95.17 | 95.86 | 95.52 | 95.57 | 106.99 |
| 41 | 95.18 | 93.84 | 94.81 | 95.36 | 97.41 | 95.91 | 95.54 | 101.98 |
| 42 | 93.43 | 90.95 | 90.25 | 94.29 | 94.46 | 94.84 | 95.21 | 110.00 |
| 43 | 96.05 | 95.60 | 94.67 | 96.80 | 94.82 | 97.60 | 98.33 | 106.85 |
| 44 | 104.15 | 105.58 | 105.08 | 104.03 | 101.22 | 104.77 | 105.02 | 111.45 |
| 45 | 84.35 | 85.74 | 89.52 | 84.69 | 84.85 | 84.81 | 83.28 | 82.12 |
| 46 | 95.27 | 100.05 | 100.49 | 95.24 | 95.10 | 95.72 | 94.77 | 89.52 |
| 47 | 93.57 | 96.19 | 91.00 | 96.20 | 90.27 | 99.71 | 96.10 | 143.28 |
| 48 | 83.81 | 88.15 | 84.05 | 85.42 | 81.91 | 88.54 | 85.21 | 126.00 |
| 49 | 100.16 | 98.64 | 94.83 | 99.85 | 93.52 | 100.33 | 100.60 | 116.53 |
| 50 | 117.11 | 92.91 | 115.43 | 119.95 | 118.08 | 119.98 | 121.85 | 138.23 |
| 51 | 111.14 | 116.04 | 111.88 | 113.92 | 112.81 | 113.71 | 115.44 | 129.92 |
| 52 | 113.47 | 94.99 | 116.70 | 115.65 | 116.42 | 115.66 | 116.65 | 127.89 |
| 53 | 89.11 | 108.00 | 90.15 | 92.06 | 93.35 | 105.74 | 95.46 | 94.25 |
| 54 | 99.05 | 109.39 | 99.44 | 102.00 | 103.54 | 116.87 | 105.84 | 102.83 |
| 55 | 97.58 | 113.01 | 99.55 | 101.18 | 102.56 | 114.57 | 103.40 | 96.54 |
| 56 | 104.27 | 108.72 | 102.13 | 107.20 | 109.85 | 129.48 | 113.06 | 112.68 |
| 57 | 100.66 | 107.01 | 102.14 | 102.23 | 107.29 | 123.58 | 108.12 | 97.30 |
| 58 | 93.24 | 93.40 | 87.18 | 94.74 | 97.40 | 107.92 | 98.82 | 98.53 |
| 59 | 118.74 | 100.50 | 119.24 | 121.16 | 119.20 | 120.79 | 122.37 | 137.58 |
| 60 | 108.11 | 114.47 | 108.69 | 107.70 | 107.45 | 109.57 | 109.35 | 110.22 |
| 61 | 109.79 | 102.50 | 109.79 | 109.59 | 109.00 | 110.71 | 110.37 | 109.99 |
| 62 | 113.52 | 119.00 | 113.39 | 112.52 | 113.20 | 113.19 | 113.44 | 109.13 |
| 63 | 116.37 | 131.35 | 113.24 | 112.40 | 111.52 | 113.67 | 124.76 | 108.72 |
| 64 | 96.14 | 119.89 | 99.79 | 95.29 | 97.29 | 97.18 | 95.56 | 90.15 |
| 65 | 82.88 | 117.10 | 95.27 | 97.96 | 95.80 | 100.71 | 101.44 | 102.94 |
| 66 | 85.65 | 115.22 | 98.38 | 98.79 | 97.71 | 100.75 | 101.52 | 98.90 |
| 67 | 78.85 | 87.73 | 92.84 | 89.77 | 90.18 | 93.45 | 94.17 | 89.61 |
| 68 | 109.80 | 118.12 | 125.57 | 130.41 | 121.52 | 125.30 | 102.36 | 112.10 |
| 69 | 119.61 | 109.93 | 118.41 | 121.22 | 112.25 | 115.96 | 96.49 | 99.53 |
| 70 | 131.71 | 119.46 | 133.40 | 133.47 | 125.05 | 127.74 | 106.29 | 108.43 |

| RECOVERY % | Group 9 | Group 10 | Group 11 | Group 12 | Group 13 | Group 14 | Group 15 | Group 16 |
|---|---|---|---|---|---|---|---|---|
| n. | 2-BUTANONE | ETHYL ACETATE | TETRAHYDROFURAN | CYCLOHEXANE | ISOPROPYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER |
| 1 | 98.90 | 97.72 | 101.39 | 127.53 | 97.73 | 122.51 | 98.39 | 102.95 |
| 2 | 86.98 | 86.30 | 89.57 | 112.59 | 89.04 | 107.78 | 87.08 | 96.43 |
| 3 | 93.22 | 92.93 | 96.32 | 120.22 | 92.78 | 116.95 | 93.67 | 100.53 |
| 4 | 96.41 | 95.62 | 98.19 | 119.32 | 98.22 | 114.32 | 95.67 | 101.40 |
| 5 | 94.05 | 93.34 | 94.90 | 108.49 | 94.65 | 104.25 | 93.06 | 96.16 |
| 6 | 97.86 | 96.80 | 98.23 | 110.06 | 97.16 | 106.24 | 96.49 | 98.64 |
| 7 | 93.92 | 92.49 | 93.40 | 101.88 | 93.37 | 98.71 | 92.08 | 93.52 |
| 8 | 95.82 | 94.56 | 96.13 | 108.58 | 95.23 | 106.50 | 94.40 | 97.49 |
| 9 | 96.71 | 95.01 | 95.04 | 98.64 | 96.84 | 94.57 | 61.93 | 93.90 |
| 10 | 101.29 | 99.34 | 98.58 | 99.56 | 102.08 | 95.19 | 98.73 | 97.06 |
| 11 | 97.82 | 96.17 | 94.07 | 91.30 | 96.33 | 90.22 | 94.04 | 92.05 |
| 12 | 101.92 | 99.89 | 97.87 | 94.96 | 100.61 | 92.46 | 98.83 | 95.83 |
| 13 | 101.14 | 98.95 | 95.93 | 87.39 | 100.66 | 83.64 | 96.94 | 91.57 |
| 14 | 102.70 | 99.79 | 95.64 | 83.44 | 101.19 | 81.60 | 99.40 | 92.53 |
| 15 | 99.66 | 98.89 | 109.72 | 137.87 | 97.19 | 129.48 | 98.02 | 106.67 |
| 16 | 85.95 | 84.85 | 93.70 | 114.10 | 82.66 | 109.11 | 85.04 | 91.42 |
| 17 | 97.88 | 96.81 | 105.29 | 124.86 | 95.55 | 118.33 | 96.25 | 101.89 |
| 18 | 88.94 | 87.24 | 94.56 | 107.91 | 86.36 | 103.82 | 95.85 | 92.27 |
| 19 | 86.36 | 84.37 | 91.35 | 101.30 | 84.72 | 98.79 | 85.86 | 88.94 |
| 20 | 89.99 | 88.07 | 94.02 | 100.48 | 88.70 | 96.44 | 88.99 | 90.41 |
| 21 | 88.95 | 87.56 | 89.86 | 96.58 | 88.64 | 93.00 | 88.71 | 89.18 |
| 22 | 91.13 | 89.73 | 90.88 | 93.49 | 90.98 | 90.51 | 91.26 | 90.44 |
| 23 | 91.65 | 89.89 | 90.54 | 90.38 | 90.56 | 88.72 | 91.52 | 89.91 |
| 24 | 98.37 | 99.69 | 103.33 | 127.43 | 100.47 | 122.81 | 101.32 | 108.48 |
| 25 | 98.85 | 99.66 | 102.28 | 118.33 | 101.53 | 116.79 | 102.94 | 108.78 |
| 26 | 85.78 | 85.95 | 89.54 | 110.01 | 87.41 | 104.91 | 88.38 | 93.80 |
| 27 | 99.77 | 99.76 | 103.01 | 123.59 | 99.38 | 120.20 | 101.81 | 107.22 |
| 28 | 100.42 | 100.52 | 102.73 | 119.11 | 102.61 | 115.26 | 102.54 | 107.17 |
| 29 | 87.14 | 86.24 | 85.86 | 89.45 | 86.90 | 91.57 | 88.67 | 90.61 |
| 30 | 94.58 | 93.07 | 89.69 | 83.12 | 93.17 | 89.76 | 96.57 | 95.88 |
| 31 | 101.99 | 100.78 | 99.47 | 101.20 | 103.80 | 100.31 | 104.30 | 104.92 |
| 32 | 92.87 | 92.76 | 94.63 | 110.26 | 94.35 | 105.72 | 93.81 | 97.97 |
| 33 | 100.53 | 99.21 | 99.68 | 105.31 | 100.78 | 102.74 | 101.98 | 102.04 |
| 34 | 103.70 | 105.68 | 110.12 | 146.13 | 104.07 | 137.32 | 107.03 | 116.03 |
| 35 | 100.61 | 101.38 | 102.60 | 123.15 | 66.28 | 182.67 | 103.53 | 109.43 |
| 36 | 98.30 | 99.04 | 98.90 | 114.21 | 101.34 | 110.71 | 102.41 | 106.92 |
| 37 | 98.47 | 98.46 | 96.78 | 106.26 | 100.26 | 106.84 | 103.70 | 106.66 |
| 38 | 98.93 | 98.39 | 95.47 | 99.21 | 100.45 | 101.55 | 103.09 | 105.76 |
| 39 | 88.72 | 89.33 | 90.79 | 111.30 | 91.50 | 104.79 | 91.98 | 97.55 |
| 40 | 94.99 | 95.35 | 95.60 | 111.98 | 97.56 | 107.29 | 98.38 | 102.57 |
| 41 | 96.50 | 95.92 | 97.29 | 107.22 | 96.92 | 105.40 | 99.41 | 102.57 |
| 42 | 93.26 | 92.81 | 96.49 | 113.97 | 94.61 | 107.07 | 95.61 | 99.75 |
| 43 | 95.19 | 95.14 | 95.41 | 101.64 | 93.30 | 100.45 | 94.48 | 94.70 |
| 44 | 102.48 | 103.15 | 103.62 | 107.29 | 101.16 | 105.11 | 101.41 | 100.71 |
| 45 | 87.06 | 86.59 | 84.57 | 80.85 | 86.40 | 82.65 | 87.43 | 84.83 |
| 46 | 97.39 | 96.77 | 94.29 | 87.38 | 95.91 | 89.52 | 96.20 | 93.35 |
| 47 | 92.97 | 126.22 | 97.03 | 243.45 | 93.23 | 142.15 | 94.36 | 97.88 |
| 48 | 85.47 | 115.53 | 88.59 | 217.35 | 86.86 | 129.39 | 87.64 | 91.29 |
| 49 | 94.68 | 94.12 | 98.15 | 110.38 | 92.97 | 105.64 | 92.01 | 94.35 |
| 50 | 115.58 | 116.33 | 117.90 | 122.81 | 116.20 | 83.65 | 113.55 | 115.01 |
| 51 | 111.45 | 111.95 | 113.36 | 116.73 | 113.47 | 79.97 | 110.37 | 111.73 |
| 52 | 115.79 | 115.81 | 115.70 | 115.68 | 117.00 | 81.60 | 115.29 | 115.86 |
| 53 | 95.42 | 99.15 | 98.82 | 88.29 | 105.36 | 66.97 | 89.87 | 102.54 |
| 54 | 104.92 | 108.72 | 108.33 | 96.32 | 112.91 | 73.27 | 97.90 | 111.50 |
| 55 | 104.03 | 107.81 | 106.34 | 90.89 | 113.43 | 70.24 | 97.87 | 110.51 |
| 56 | 107.19 | 110.77 | 114.11 | 104.03 | 119.09 | 76.92 | 102.18 | 108.22 |
| 57 | 105.46 | 108.82 | 109.06 | 91.56 | 116.32 | 70.86 | 100.60 | 104.67 |
| 58 | 94.41 | 95.73 | 98.84 | 90.48 | 102.52 | 65.08 | 86.16 | 97.26 |
| 59 | 117.82 | 118.69 | 119.72 | 123.09 | 120.17 | 84.44 | 115.40 | 117.12 |
| 60 | 108.56 | 108.92 | 108.58 | 109.14 | 105.89 | 109.55 | 107.14 | 106.67 |
| 61 | 109.34 | 109.80 | 109.16 | 108.59 | 110.02 | 107.33 | 108.02 | 107.62 |
| 62 | 112.64 | 112.52 | 111.27 | 107.97 | 111.21 | 110.00 | 111.31 | 110.26 |
| 63 | 114.91 | 114.71 | 112.60 | 107.13 | 110.38 | 103.34 | 110.69 | 106.24 |
| 64 | 98.23 | 97.76 | 95.62 | 90.30 | 97.34 | 92.57 | 97.33 | 96.69 |
| 65 | 100.78 | 101.13 | 101.14 | 102.32 | 101.78 | 101.32 | 99.88 | 100.84 |
| 66 | 102.12 | 102.18 | 101.07 | 98.95 | 105.82 | 98.44 | 101.30 | 101.13 |
| 67 | 95.90 | 95.97 | 94.15 | 90.06 | 97.09 | 92.43 | 94.90 | 94.88 |
| 68 | 122.06 | 126.22 | 121.30 | 115.01 | 125.36 | 114.90 | 122.12 | 119.11 |
| 69 | 111.08 | 114.57 | 109.73 | 102.49 | 114.24 | 102.41 | 110.87 | 107.57 |
| 70 | 125.53 | 129.33 | 122.55 | 113.15 | 127.32 | 115.85 | 125.27 | 121.61 |

| RECOVERY % | Group 17 | Group 18 | Group 19 | Group 20 | Group 21 | Group 22 | Group 23 | Group 24 |
|---|---|---|---|---|---|---|---|---|
| EXPERIMENTS | TOLUENE | BUTYL ACETATE | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
| 1 | 102.41 | 97.35 | 100.28 | 85.25 | 84.48 | 104.35 | 102.88 | 96.85 |
| 2 | 92.84 | 87.65 | 87.16 | 94.69 | 94.62 | 113.05 | 86.49 | 81.04 |
| 3 | 99.19 | 93.81 | 93.33 | 88.28 | 87.50 | 102.94 | 106.72 | 99.45 |
| 4 | 100.74 | 95.88 | 95.96 | 92.36 | 90.77 | 105.56 | 102.69 | 95.95 |
| 5 | 95.87 | 93.02 | 93.84 | 93.84 | 91.98 | 101.51 | 90.40 | 83.38 |
| 6 | 97.81 | 95.39 | 95.91 | 97.80 | 95.62 | 102.94 | 96.03 | 87.31 |
| 7 | 93.36 | 91.85 | 92.69 | 83.01 | 81.39 | 88.48 | 92.86 | 85.68 |
| 8 | 96.69 | 94.14 | 99.79 | 109.17 | 85.36 | 88.45 | 108.37 | 98.17 |
| 9 | 93.57 | 93.23 | 94.84 | 87.89 | 85.73 | 87.32 | 104.95 | 96.84 |
| 10 | 97.28 | 97.94 | 100.18 | 117.61 | 114.19 | 110.97 | 89.87 | 81.93 |
| 11 | 92.49 | 93.22 | 94.72 | 108.21 | 105.21 | 100.97 | 89.29 | 80.54 |
| 12 | 96.19 | 98.11 | 101.34 | 90.95 | 89.29 | 82.53 | 93.05 | 83.87 |
| 13 | 92.58 | 95.43 | 98.72 | 106.33 | 104.12 | 86.66 | 108.05 | 95.94 |
| 14 | 93.66 | 98.98 | 103.79 | 102.80 | 101.51 | 80.16 | 95.38 | 88.89 |
| 15 | 105.13 | 96.17 | 93.91 | 100.14 | 96.14 | 124.52 | 94.09 | 85.39 |
| 16 | 90.49 | 83.96 | 83.16 | 81.14 | 79.60 | 100.49 | 83.22 | 74.67 |
| 17 | 101.55 | 94.54 | 93.55 | 83.47 | 80.59 | 101.28 | 105.00 | 91.61 |
| 18 | 91.88 | 87.51 | 88.23 | 91.09 | 88.76 | 108.67 | 94.04 | 82.97 |
| 19 | 89.07 | 85.71 | 86.49 | 81.41 | 80.00 | 94.26 | 89.87 | 84.70 |
| 20 | 90.96 | 88.74 | 90.07 | 92.89 | 91.37 | 103.37 | 89.83 | 82.45 |
| 21 | 89.77 | 88.72 | 90.79 | 112.04 | 113.10 | 101.37 | 104.19 | 103.22 |
| 22 | 91.13 | 91.39 | 94.07 | 95.10 | 95.08 | 80.67 | 95.02 | 93.83 |
| 23 | 90.82 | 92.31 | 95.09 | 98.61 | 98.81 | 78.94 | 118.94 | 117.79 |
| 24 | 108.27 | 102.14 | 101.85 | 109.68 | 110.41 | 108.15 | 101.28 | 100.75 |
| 25 | 109.04 | 105.56 | 106.37 | 97.91 | 98.16 | 94.88 | 104.37 | 108.08 |
| 26 | 94.02 | 89.42 | 89.92 | 100.42 | 100.50 | 95.18 | 96.99 | 100.97 |
| 27 | 107.58 | 102.51 | 103.71 | 107.25 | 107.44 | 99.24 | 98.60 | 105.00 |
| 28 | 107.62 | 103.75 | 105.32 | 119.03 | 119.95 | 103.59 | 92.29 | 105.72 |
| 29 | 90.86 | 90.26 | 92.77 | 118.41 | 118.36 | 97.52 | 88.55 | 105.47 |
| 30 | 96.86 | 99.74 | 103.63 | 119.05 | 118.54 | 109.24 | 108.21 | 109.32 |
| 31 | 105.82 | 107.33 | 110.40 | 109.50 | 109.93 | 96.71 | 122.21 | 136.53 |
| 32 | 98.20 | 91.95 | 96.38 | 107.21 | 107.29 | 89.85 | 98.18 | 114.68 |
| 33 | 103.88 | 102.93 | 104.14 | 109.37 | 110.89 | 78.94 | 82.00 | 111.79 |
| 34 | 115.01 | 107.10 | 107.39 | 84.48 | 82.30 | 92.41 | 97.79 | 100.24 |
| 35 | 109.69 | 104.39 | 106.93 | 102.44 | 99.82 | 99.74 | 93.81 | 109.63 |
| 36 | 106.97 | 104.97 | 106.81 | 114.27 | 113.01 | 107.56 | 81.83 | 102.23 |
| 37 | 106.52 | 106.32 | 109.08 | 95.99 | 94.92 | 96.04 | 96.81 | 101.56 |
| 38 | 105.84 | 107.20 | 110.58 | 114.27 | 113.01 | 107.56 | 81.83 | 102.23 |
| 39 | 97.20 | 94.26 | 96.40 | 102.70 | 103.40 | 83.87 | 104.97 | 111.76 |
| 40 | 102.58 | 100.75 | 102.47 | 112.09 | 112.67 | 101.61 | 107.17 | 115.53 |
| 41 | 102.58 | 101.94 | 104.80 | 89.32 | 86.43 | 91.81 | 87.48 | 88.97 |
| 42 | 99.55 | 96.77 | 98.28 | 109.42 | 106.01 | 104.60 | 96.10 | 103.33 |
| 43 | 94.83 | 94.31 | 93.01 | 91.65 | 89.20 | 96.89 | 100.02 | 108.07 |
| 44 | 100.08 | 98.92 | 96.64 | 97.39 | 97.51 | 98.12 | 99.12 | 108.33 |
| 45 | 85.14 | 86.96 | 87.02 | 98.83 | 99.97 | 98.90 | 65.22 | 74.08 |
| 46 | 93.07 | 95.78 | 96.47 | 88.87 | 89.04 | 86.78 | 77.72 | 99.12 |
| 47 | 96.41 | 90.10 | 87.82 | 115.78 | 114.20 | 105.45 | 91.71 | 99.26 |
| 48 | 89.92 | 85.86 | 84.24 | 81.39 | 81.17 | 88.96 | 97.64 | 97.84 |
| 49 | 93.26 | 89.63 | 87.05 | 92.24 | 92.49 | 103.05 | 70.07 | 70.67 |
| 50 | 114.21 | 110.85 | 110.17 | 102.47 | 102.16 | 111.30 | 104.71 | 97.94 |
| 51 | 111.26 | 108.61 | 109.56 | 89.83 | 89.91 | 96.89 | 102.79 | 99.08 |
| 52 | 115.68 | 114.91 | 115.31 | 88.07 | 88.18 | 94.53 | 91.53 | 87.51 |
| 53 | 104.15 | 102.67 | 96.77 | 85.35 | 85.04 | 90.14 | 82.89 | 82.36 |
| 54 | 113.45 | 111.09 | 104.79 | 94.69 | 94.03 | 98.61 | 96.94 | 92.47 |
| 55 | 112.49 | 112.59 | 107.35 | 97.78 | 97.22 | 101.58 | 86.39 | 86.06 |
| 56 | 115.48 | 111.61 | 106.56 | 105.56 | 104.92 | 108.77 | 98.55 | 97.69 |
| 57 | 113.09 | 115.28 | 112.16 | 109.48 | 108.75 | 111.03 | 93.84 | 94.72 |
| 58 | 98.48 | 96.36 | 92.17 | 109.44 | 108.63 | 110.20 | 101.16 | 100.55 |
| 59 | 116.94 | 113.81 | 113.65 | 112.89 | 112.69 | 112.26 | 98.03 | 100.23 |
| 60 | 107.20 | 107.79 | 107.51 | 113.60 | 113.90 | 110.36 | 92.81 | 99.19 |
| 61 | 107.79 | 108.54 | 108.72 | 114.85 | 114.36 | 110.43 | 113.23 | 119.47 |
| 62 | 110.50 | 112.46 | 112.05 | 110.95 | 111.15 | 103.36 | 103.49 | 113.04 |
| 63 | 109.69 | 110.91 | 114.39 | 122.96 | 124.11 | 110.74 | 113.33 | 128.10 |
| 64 | 96.83 | 100.17 | 99.73 | 121.66 | 122.56 | 106.11 | 93.09 | 110.95 |
| 65 | 101.01 | 100.40 | 86.07 | 99.20 | 96.51 | 98.17 | 89.53 | 85.61 |
| 66 | 101.87 | 103.10 | 89.13 | 93.54 | 94.59 | 92.63 | 91.54 | 98.42 |
| 67 | 95.52 | 97.75 | 83.10 | 96.71 | 97.65 | 95.38 | 110.80 | 112.14 |
| 68 | 117.01 | 123.81 | 123.14 | 93.77 | 93.13 | 99.00 | 99.88 | 100.33 |
| 69 | 105.65 | 112.27 | 111.84 | 87.77 | 87.98 | 91.57 | 97.42 | 99.51 |
| 70 | 119.49 | 128.77 | 129.36 | 71.80 | 71.74 | 75.11 | 96.80 | 98.60 |

| | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 | Group 7 | Group 8 |
|---|---|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHYL ACETATE | DICHLOROMETANE | HEXANE |
| DIMENSION | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 |
| MEAN | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 | 100.98 | 107.81 |
| STD DEV. | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 | 8.76 | 14.57 |
| CONFIDENCE 99% | 3.03 | 3.21 | 3.12 | 3.08 | 2.86 | 3.18 | 2.70 | 4.48 |
| L 1 | 95.53 | 99.20 | 95.68 | 98.59 | 97.31 | 99.54 | 98.98 | 104.17 |
| L 2 | 101.60 | 103.89 | 100.46 | 103.06 | 101.46 | 104.31 | 102.97 | 111.45 |
| LCL | 95.03 | 97.80 | 94.44 | 97.24 | 96.05 | 98.22 | 97.84 | 102.58 |
| UCL | 102.10 | 105.29 | 101.71 | 104.41 | 102.72 | 105.64 | 104.12 | 113.03 |

| | Group 9 | Group 10 | Group 11 | Group 12 | Group 13 | Group 14 | Group 15 | Group 16 |
|---|---|---|---|---|---|---|---|---|
| | 2-BUTANONE | ETHYL ACETATE | TETRAHYDROFURAN | CYCLOHEXANE | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER |
| DIMENSION | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 |
| MEAN | 99.16 | 100.07 | 100.15 | 109.79 | 99.68 | 101.90 | 98.30 | 101.14 |
| STD DEV. | 8.77 | 10.22 | 8.65 | 24.73 | 10.68 | 18.66 | 9.50 | 8.27 |
| CONFIDENCE 99% | 2.70 | 3.15 | 2.66 | 7.61 | 3.29 | 5.75 | 2.93 | 2.55 |
| L 1 | 96.99 | 97.72 | 98.19 | 104.04 | 97.09 | 97.64 | 96.03 | 99.23 |
| L 2 | 101.33 | 102.42 | 102.11 | 115.55 | 102.26 | 106.16 | 100.58 | 103.04 |
| LCL | 96.02 | 96.40 | 97.05 | 100.93 | 95.85 | 95.21 | 94.90 | 98.17 |
| UCL | 102.31 | 103.73 | 103.25 | 118.66 | 103.51 | 108.59 | 101.71 | 104.10 |

| | Group 17 | Group 18 | Group 19 | Group 20 | Group 21 | Group 22 | Group 23 | Group 24 |
|---|---|---|---|---|---|---|---|---|
| | TOLUENE | BUTHYL ACETATE | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
| DIMENSION | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 | 70.00 |
| MEAN | 101.34 | 99.99 | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV. | 8.45 | 9.36 | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| CONFIDENCE 99% | 2.60 | 2.88 | 2.99 | 3.62 | 3.74 | 3.02 | 3.11 | 3.85 |
| L 1 | 99.37 | 97.79 | 97.67 | 97.41 | 95.32 | 95.79 | 93.31 | 94.83 |
| L 2 | 103.32 | 102.20 | 102.07 | 102.74 | 102.71 | 101.76 | 99.32 | 101.39 |
| LCL | 98.31 | 96.64 | 96.39 | 95.86 | 94.65 | 95.26 | 92.69 | 93.62 |
| UCL | 104.37 | 103.35 | 103.35 | 104.30 | 103.38 | 102.29 | 99.94 | 102.60 |

| | GENERAL |
|---|---|
| DIMENSION | 1680 |
| MEAN | 100.53 |
| STD DEV. | 3.67 |
| GROUPS | 24 |

## A6. Reproducibility Tests

| GC-FID_Control | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE |
| 1 | 100.95 | 99.73 | 99.51 | 104.22 | 100.71 | 101.72 |
| 2 | 88.71 | 90.58 | 89.19 | 91.70 | 90.61 | 88.25 |
| 3 | 105.04 | 108.51 | 109.15 | 108.76 | 109.09 | 104.19 |
| 4 | 108.29 | 113.13 | 114.19 | 111.52 | 112.89 | 105.94 |
| 5 | 114.52 | 119.49 | 119.46 | 118.03 | 118.45 | 112.70 |
| 6 | 85.44 | 82.66 | 83.10 | 88.30 | 83.04 | 87.02 |
| 7 | 88.73 | 84.71 | 85.20 | 91.84 | 86.57 | 90.74 |

| GC-FID_Control | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 98.81 | 99.83 | 99.97 | 102.05 | 100.19 | 98.65 |
| STANDARD DEVIATION | 11.27 | 14.42 | 14.64 | 11.51 | 13.82 | 9.97 |
| | | | | | | |
| MEAN_all | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 |
| STD DEV_all | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 |
| TEST Z (Z=2.2326) | 0.01 | -0.06 | 0.07 | 0.05 | 0.03 | -0.12 |

| GC-FID_Control | Group 7 | Group 8 | Group 9 | Group 10 | Group 11 | Group 12 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
| 1 | 107.21 | 119.62 | 101.18 | 101.64 | 103.73 | 121.29 |
| 2 | 92.17 | 85.33 | 88.87 | 88.28 | 86.59 | 85.80 |
| 3 | 108.40 | 92.17 | 107.61 | 106.33 | 101.67 | 93.94 |
| 4 | 110.07 | 84.20 | 110.91 | 108.92 | 101.78 | 86.03 |
| 5 | 117.15 | 93.33 | 116.61 | 114.74 | 108.60 | 94.06 |
| 6 | 90.75 | 105.08 | 72.15 | 88.25 | 53.49 | 106.83 |
| 7 | 94.76 | 111.89 | 73.90 | 90.63 | 55.34 | 113.59 |

| GC-FID_Control | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 102.93 | 98.80 | 95.89 | 99.83 | 87.32 | 100.22 |
| STANDARD DEVIATION | 10.26 | 13.62 | 17.87 | 10.82 | 23.47 | 13.86 |
| | | | | | | |
| MEAN_all | 100.98 | 107.81 | 99.16 | 100.07 | 100.15 | 109.79 |
| STD DEV_all | 8.76 | 14.57 | 8.77 | 10.22 | 8.65 | 24.73 |
| TEST Z (Z=2.2326) | 0.08 | -0.23 | -0.14 | -0.01 | -0.56 | -0.15 |

| GC-FID_Control | Group 13 | Group 14 | Group 15 | Group 16 | Group 17 | Group 18 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHYL ACETATE |
| 1 | 103.34 | 118.98 | 101.52 | 108.29 | 106.94 | 101.36 |
| 2 | 89.78 | 85.31 | 87.90 | 87.62 | 87.41 | 88.00 |
| 3 | 109.00 | 96.49 | 106.54 | 104.77 | 104.72 | 107.75 |
| 4 | 112.08 | 89.94 | 109.93 | 105.21 | 105.77 | 112.59 |
| 5 | 117.80 | 95.74 | 115.58 | 109.90 | 110.83 | 116.97 |
| 6 | 88.70 | 107.93 | 88.32 | 95.37 | 94.28 | 88.30 |
| 7 | 91.02 | 114.06 | 90.82 | 99.06 | 97.83 | 89.89 |

| GC-FID_Control | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 101.67 | 101.21 | 100.09 | 101.46 | 101.11 | 100.69 |
| STANDARD DEVIATION | 11.89 | 12.64 | 11.21 | 7.93 | 8.25 | 12.17 |
| | | | | | | |
| MEAN_all | 99.68 | 101.90 | 98.30 | 101.14 | 101.34 | 99.99 |
| STD DEV_all | 10.68 | 18.66 | 9.50 | 8.27 | 8.45 | 9.36 |
| TEST Z (Z=2.2326) | 0.07 | -0.01 | 0.07 | 0.01 | -0.01 | 0.03 |

| GC-FID_Control | Group 19 | Group 20 | Group 21 | Group 22 | Group 23 | Group 24 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
| 1 | 100.37 | 77.90 | 77.51 | 88.84 | 90.99 | 91.34 |
| 2 | 88.64 | 93.59 | 93.69 | 91.63 | 102.44 | 102.70 |
| 3 | 108.76 | 102.82 | 103.90 | 95.67 | 104.23 | 105.24 |
| 4 | 114.77 | 112.83 | 113.62 | 101.90 | 116.66 | 117.41 |
| 5 | 119.36 | 135.95 | 137.41 | 110.50 | 120.12 | 120.97 |
| 6 | 87.45 | 72.87 | 72.90 | 86.58 | 88.67 | 90.21 |
| 7 | 88.80 | 82.98 | 83.74 | 88.35 | 88.67 | 90.21 |

| GC-FID_Control | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 101.16 | 96.99 | 97.54 | 94.78 | 101.68 | 102.58 |
| STANDARD DEVIATION | 13.37 | 22.20 | 22.74 | 8.68 | 13.07 | 12.89 |
| | | | | | | |
| MEAN_all | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV_all | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| TEST Z (Z=2.2326) | 0.05 | -0.10 | -0.05 | -0.15 | 0.20 | 0.14 |

| GC-FID_Principal | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 | Group 6 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE |
| 1 | 91.22 | 95.85 | 91.71 | 95.78 | 91.21 | 94.81 |
| 2 | 98.62 | 112.90 | 96.33 | 102.46 | 98.60 | 99.70 |
| 3 | 100.83 | 104.68 | 98.46 | 104.50 | 100.93 | 101.03 |
| 4 | 104.72 | 107.51 | 102.99 | 108.82 | 105.24 | 104.40 |
| 5 | 105.62 | 108.10 | 102.18 | 109.10 | 105.48 | 102.73 |
| 6 | 86.25 | 89.65 | 81.71 | 87.04 | 84.05 | 88.71 |
| 7 | 102.61 | 115.12 | 94.53 | 103.54 | 98.73 | 105.01 |

| GC-FID_Principal | METHANOL | ETHANOL | ISOPROPANOL | ACETONE | ACETONITRILE | METHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 98.55 | 104.83 | 95.42 | 101.61 | 97.75 | 99.49 |
| STANDRD DEVIATION | 7.24 | 9.13 | 7.25 | 7.82 | 7.72 | 5.86 |
| | | | | | | |
| MEAN_all | 98.57 | 101.55 | 98.07 | 100.83 | 99.39 | 101.93 |
| STD DEV_all | 9.85 | 10.43 | 10.14 | 10.00 | 9.30 | 10.34 |
| TEST Z (Z=2.2326) | 0.00 | 0.12 | -0.10 | 0.03 | -0.07 | -0.09 |

| GC-FID_Principal | Group 7 | Group 8 | Group 9 | Group 10 | Group 11 | Group 12 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
| 1 | 99.30 | 118.76 | 93.22 | 92.93 | 96.32 | 120.22 |
| 2 | 103.64 | 99.66 | 96.71 | 95.01 | 95.04 | 98.64 |
| 3 | 104.49 | 91.67 | 97.82 | 96.17 | 94.07 | 91.30 |
| 4 | 108.11 | 96.23 | 101.92 | 99.89 | 97.87 | 94.96 |
| 5 | 108.32 | 89.13 | 101.14 | 98.95 | 95.93 | 87.39 |
| 6 | 89.20 | 113.97 | 85.95 | 84.85 | 93.70 | 114.10 |
| 7 | 105.85 | 138.66 | 99.66 | 98.89 | 109.72 | 137.87 |

| GC-FID_Principal | DICHLOROMETANE | HEXANE | 2-BUTANONE | ETHYL LACETATE | TETRAHYDROFURAN | CYCLOHEXANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 102.70 | 106.87 | 96.63 | 95.24 | 97.52 | 106.35 |
| STANDRD DEVIATION | 6.69 | 17.86 | 5.55 | 5.21 | 5.56 | 18.35 |
| | | | | | | |
| MEAN_all | 100.98 | 107.81 | 99.16 | 100.07 | 100.15 | 109.79 |
| STD DEV_all | 8.76 | 14.57 | 8.77 | 10.22 | 8.65 | 24.73 |
| TEST Z (Z=2.2326) | 0.07 | -0.02 | -0.11 | -0.18 | -0.11 | -0.05 |

| GC-FID_Principal | Group 13 | Group 14 | Group 15 | Group 16 | Group 17 | Group 18 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHY LACETATE |
| 1 | 92.78 | 116.95 | 93.67 | 100.53 | 99.19 | 93.81 |
| 2 | 96.84 | 94.57 | 61.93 | 93.90 | 93.57 | 93.23 |
| 3 | 96.33 | 90.22 | 94.04 | 92.05 | 92.49 | 93.22 |
| 4 | 100.61 | 92.46 | 98.83 | 95.83 | 96.19 | 98.11 |
| 5 | 100.66 | 83.64 | 96.94 | 91.57 | 92.58 | 95.43 |
| 6 | 82.66 | 109.11 | 85.04 | 91.42 | 90.49 | 83.96 |
| 7 | 97.19 | 129.48 | 98.02 | 106.67 | 105.13 | 96.17 |

| GC-FID_Principal | ISOPROPHYL ACETATE | HEPTANE | 1,4-DIOXAN | CYCLOPENTYL METHYL ETHER | TOLUENE | BUTHY LACETATE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 95.30 | 102.35 | 89.78 | 96.00 | 95.66 | 93.42 |
| STANDRD DEVIATION | 6.19 | 16.58 | 13.12 | 5.70 | 5.05 | 4.53 |
| | | | | | | |
| MEAN_all | 99.68 | 101.90 | 98.30 | 101.14 | 101.34 | 99.99 |
| STD DEV_all | 10.68 | 18.66 | 9.50 | 8.27 | 8.45 | 9.36 |
| TEST Z (Z=2.2326) | -0.16 | 0.01 | -0.34 | -0.23 | -0.25 | -0.27 |

| GC-FID_Principal | Group 19 | Group 20 | Group 21 | Group 22 | Group 23 | Group 24 |
|---|---|---|---|---|---|---|
| EXPERIMENTS | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
| 1 | 93.33 | 88.28 | 87.50 | 102.94 | 106.72 | 99.45 |
| 2 | 94.84 | 87.89 | 85.73 | 87.32 | 104.95 | 96.84 |
| 3 | 94.72 | 108.21 | 105.21 | 100.97 | 89.29 | 80.54 |
| 4 | 101.34 | 90.95 | 89.29 | 82.53 | 93.05 | 83.87 |
| 5 | 98.72 | 106.33 | 104.12 | 86.66 | 108.05 | 95.94 |
| 6 | 83.16 | 81.14 | 79.60 | 100.49 | 83.22 | 74.67 |
| 7 | 93.91 | 92.89 | 91.37 | 103.37 | 89.83 | 82.45 |

| GC-FID_Principal | DIMETHYLFORMAMIDE | 2-BUTANOL | 1-BUTANOL | PYRIDINE | DIISOPROPYL ETHER | OCTANE |
|---|---|---|---|---|---|---|
| DIMENSION | 7 | 7 | 7 | 7 | 7 | 7 |
| MEAN | 94.29 | 93.67 | 91.83 | 94.90 | 96.45 | 87.68 |
| STANDRD DEVIATION | 5.70 | 9.99 | 9.51 | 8.97 | 9.95 | 9.60 |
| | | | | | | |
| MEAN_all | 99.87 | 100.08 | 99.02 | 98.78 | 96.31 | 98.11 |
| STD DEV_all | 9.70 | 11.76 | 12.16 | 9.81 | 10.10 | 12.52 |
| TEST Z (Z=2.2326) | -0.22 | -0.21 | -0.22 | -0.15 | 0.00 | -0.31 |

## A7. Experiments on Laboratory Control Sample, Matrix Spike (MS) and Matrix Spike Duplicate (MSD)

- Laboratory Control Sample

| EXPERIMENTS | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| 1 | 116.37 | 108.65 | 110.50 | 108.01 | 113.17 | 109.84 |
| 2 | 99.88 | 122.82 | 96.86 | 94.12 | 98.79 | 96.77 |
| 3 | 111.35 | 130.43 | 103.24 | 100.92 | 105.21 | 101.14 |
| 4 | 112.37 | 93.82 | 100.74 | 96.41 | 102.75 | 100.89 |
| 5 | 109.88 | 117.37 | 94.27 | 89.54 | 97.58 | 96.03 |
| 6 | 119.42 | 114.38 | 108.38 | 99.49 | 110.54 | 104.15 |
| 7 | 111.37 | 112.56 | 88.41 | 83.26 | 93.35 | 90.07 |
| 8 | 105.82 | 96.69 | 92.59 | 88.59 | 93.50 | 94.19 |
| 9 | 96.94 | 96.43 | 92.33 | 87.28 | 91.05 | 93.58 |
| 10 | 104.16 | 102.62 | 93.76 | 87.81 | 93.27 | 96.59 |
| 11 | 116.75 | 113.14 | 108.34 | 106.62 | 107.97 | 101.28 |
| 12 | 120.97 | 125.23 | 121.23 | 119.06 | 111.86 | 108.84 |
| 13 | 118.48 | 121.57 | 107.23 | 109.26 | 106.54 | 103.39 |
| 14 | 120.09 | 117.25 | 121.85 | 109.42 | 104.68 | 103.57 |
| 15 | 102.16 | 119.75 | 109.86 | 113.48 | 115.79 | 99.46 |
| 16 | 102.46 | 117.39 | 111.63 | 116.08 | 115.16 | 105.59 |
| 17 | 107.20 | 120.21 | 110.81 | 101.01 | 111.86 | 139.48 |
| 18 | 104.65 | 109.32 | 116.50 | 96.25 | 106.85 | 117.77 |
| 19 | 90.56 | 120.24 | 113.32 | 103.01 | 113.77 | 111.94 |
| 20 | 75.90 | 116.17 | 110.45 | 101.54 | 111.91 | 109.68 |

| | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
| DIMENSION | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| AVERAGE VALUE | 107.34 | 113.80 | 105.61 | 100.56 | 105.28 | 104.21 |
| STANDRD DEVIATION | 11.14 | 9.94 | 9.86 | 10.22 | 8.10 | 10.81 |
| RSD% | 10.37 | 8.73 | 9.34 | 10.16 | 7.70 | 10.37 |

- Matrix Spike (MS)

| EXPERIMENTS | METHANOL | ETHANOL | ISOPROPANOL | ACETONITRILE | ETHYL ACETATE | TOLUENE |
|---|---|---|---|---|---|---|
| **1** | 121.40 | 134.87 | 111.68 | 119.51 | 84.81 | 118.70 |
| **2** | 118.57 | 139.47 | 110.62 | 119.78 | 85.42 | 111.26 |
| **3** | 124.29 | 141.76 | 111.82 | 125.30 | 89.55 | 117.13 |
| **4** | 129.61 | 148.47 | 109.73 | 129.47 | 91.91 | 119.21 |
| **5** | 121.69 | 124.68 | 112.32 | 121.47 | 87.20 | 113.48 |
| **6** | 123.56 | 129.75 | 120.97 | 123.78 | 88.41 | 114.57 |
| **7** | 136.21 | 133.71 | 135.46 | 137.32 | 98.28 | 126.04 |
| **8** | 204.58 | 138.65 | 212.94 | 204.46 | 150.47 | 210.42 |
| **9** | 97.61 | 154.22 | 100.83 | 97.51 | 70.69 | 99.23 |
| **10** | 106.35 | 104.94 | 108.12 | 106.49 | 76.80 | 105.79 |
| **11** | 105.40 | 112.75 | 108.52 | 105.49 | 74.26 | 103.73 |
| **12** | 113.95 | 114.67 | 116.54 | 114.55 | 80.99 | 109.55 |
| **13** | 118.51 | 126.63 | 122.24 | 119.47 | 83.88 | 112.38 |
| **14** | 70.16 | 73.62 | 68.70 | 69.00 | 47.30 | 61.98 |
| **15** | 104.83 | 111.22 | 110.62 | 107.55 | 74.85 | 95.11 |
| **16** | 103.56 | 95.58 | 116.07 | 106.45 | 80.31 | 105.66 |
| **17** | 107.52 | 94.67 | 110.12 | 97.44 | 78.07 | 107.38 |
| **18** | 115.96 | 104.68 | 120.64 | 107.05 | 84.87 | 117.97 |
| **19** | 106.42 | 107.78 | 111.37 | 97.31 | 78.19 | 108.30 |
| **20** | 115.39 | 125.36 | 122.16 | 106.13 | 85.51 | 117.92 |

| ANOVA | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | **METHANOL** | **ETHANOL** | **ISOPROPANOL** | **ACETONITRILE** | **ETHYL ACETATE** | **TOLUENE** |
| **DIMENSION** | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| **AVERAGE VALUE** | 117.28 | 120.87 | 117.07 | 115.78 | 84.59 | 113.79 |
| **STANDRD DEVIATION** | 24.82 | 20.42 | 25.82 | 25.61 | 18.62 | 26.32 |
| **RSD %** | 21.16 | 16.89 | 22.05 | 22.12 | 22.02 | 23.13 |

- Matrix Spike Duplicate (MSD)

| ANOVA | GROUPS - MATRIX SPIKE DUPLICATE | | | | | |
|---|---|---|---|---|---|---|
| **EXPERIMENTS** | **METHANOL** | **ETHANOL** | **ISOPROPANOL** | **ACETONITRILE** | **ETHYL ACETATE** | **TOLUENE** |
| **1** | 129.59 | 147.66 | 116.83 | 125.46 | 89.07 | 126.21 |
| **2** | 123.28 | 140.53 | 114.93 | 122.68 | 87.31 | 114.50 |
| **3** | 112.36 | 127.24 | 99.13 | 112.19 | 79.87 | 104.03 |
| **4** | 128.21 | 132.80 | 108.84 | 130.29 | 91.55 | 120.29 |
| **5** | 121.26 | 128.78 | 112.57 | 121.69 | 85.99 | 112.96 |
| **6** | 126.77 | 133.63 | 123.25 | 126.18 | 89.66 | 116.08 |
| **7** | 130.85 | 121.71 | 129.50 | 131.68 | 94.17 | 120.13 |
| **8** | 196.91 | 123.96 | 205.60 | 197.78 | 145.89 | 204.28 |
| **9** | 100.36 | 159.08 | 103.87 | 91.13 | 72.74 | 102.70 |
| **10** | 105.84 | 111.15 | 108.37 | 96.35 | 76.98 | 107.87 |
| **11** | 108.08 | 108.48 | 110.42 | 98.19 | 78.06 | 104.27 |
| **12** | 75.92 | 127.41 | 116.79 | 114.22 | 81.57 | 99.47 |
| **13** | 121.15 | 136.83 | 122.35 | 121.27 | 85.07 | 112.49 |
| **14** | 75.92 | 75.01 | 73.40 | 74.45 | 51.18 | 66.67 |
| **15** | 115.39 | 113.88 | 122.16 | 117.42 | 82.99 | 105.72 |
| **16** | 120.36 | 117.43 | 133.94 | 123.97 | 92.62 | 121.29 |
| **17** | 101.66 | 110.19 | 106.91 | 92.81 | 76.03 | 104.09 |
| **18** | 116.47 | 106.92 | 118.97 | 105.67 | 84.33 | 116.59 |
| **19** | 114.74 | 110.28 | 122.16 | 104.58 | 83.30 | 114.91 |
| **20** | 113.15 | 119.19 | 118.95 | 103.81 | 83.64 | 114.45 |

| ANOVA | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| | **METHANOL** | **ETHANOL** | **ISOPROPANOL** | **ACETONITRILE** | **ETHYL ACETATE** | **TOLUENE** |
| **DIMENSION** | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 | 20.00 |
| **AVERAGE VALUE** | 116.91 | 122.61 | 118.45 | 115.59 | 85.60 | 114.45 |
| **STANDRD DEVIATION** | 24.26 | 17.85 | 24.15 | 24.59 | 16.96 | 24.52 |
| **RSD %** | 20.75 | 14.56 | 20.39 | 21.27 | 19.81 | 21.42 |

**BIBLIOGRAPHY**


1. Decreto Legislativo 3 aprile 2006, n. 152
2. Directive 2008/1/EC on Integrated Pollution Prevention and Control (IPPC Directive)
3. Regulation (EC) No 1272/2008 of the parliament and of the council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006, Official Journal of the European Union L 353/1
4. Pooya Azadi, Robert Malina, Steven R.H. Barrett, Markus Kraft, The evolution of the biofuel science, *Renewable and Sustainable Energy Reviews 76 (2017) 1479–1484*
5. Augustine Quek , Rajasekhar Balasubramanian, Life Cycle Assessment of Energy and Energy Carriers from Waste Matter e A Review, *Journal of Cleaner Production 79 (2014) 18 - 31*
6. Adeel Tariq, Yuosre F. Badi, Waqas Tariq, Umair Saeed Bhutta, Drivers and consequences of green product and process innovation: A systematic review, conceptual framework, and future outlook, *Technology in Society 51 (2017) 8-23*
7. M.A.Curran, Life Cycle Assessment: Principles and Practices, United States Environmental Protection Agency, National Risk Management Research Laboratory, Cincinnati, Ohio, 2006
8. Michael J. Raymond, C. Stewart Slater and Mariano J. Savelski, LCA approach to the analysis of solvent waste issues in the pharmaceutical Industry, *GreenChem., 2010,12, 1826–1834*
9. Analytical procedures for quality control of pharmaceuticals in terms of residual solvents content: Challenges and recent developments, MaciejTankiewicz, Jacek Namies´nik, WiesławSawick, *Trends in Analytical hemistry 80 (2016) 328–344*
10. ICH guideline Q3C (R6) on impurities: guideline for residual solvents EMA/CHMP/ICH/82260/2006
11. Eduardo J., Cavanagh, Mariano J.Savelski, C.Stewart Slater, Optimization of environmental impact reduction and economic feasibility of solventwasterecovery using a new software tool, *Chemical Engineering Research and Design, 9 2 ( 2 0 1 4 ) 1942–1954*
12. Abejon R., Garea A., Irabien A., 2015, Organic solvent recovery and reuse in pharmaceutical purification processes by nanofiltration membrane cascades, *Chemical Engineering Transactions, 43, 1057-1062 DOI: 10.3303/CET1543177*
13. Verónica García, Eva Pongrácz, Paul S. Phillips, Riitta L. Keiski, From waste treatment to resource efficiency in the chemical industry: recovery of organic solvents from waters containing electrolytes by pervaporation, *Journal of Cleaner Production 39 (2013) 146e153*
14. Ruth Barro, Jorge Regueiro, MaríaLlompart, Carmen Garcia-Jares, Analysis of industrial contaminants in indoor air: Part 1. Volatile organic compounds, carbonyl compounds, polycyclic aromatic hydrocarbons and polychlorinated biphenyls, *Journal of Chromatography A, 1216 (2009) 540–566*
15. Jo Dewulf, Herman Van Langenhove, Anthropogenic volatile organic compounds in ambient air and natural waters: a review on recent developments of analytical methodology, performance and interpretation of field measurements, *Journal of Chromatography A, 843 (1999) 163–177*

16. Kristof Demeestere, Jo Dewulf, Bavo De Witte, Herman Van Langenhove, Sample preparation for the analysis of volatile organic compounds in air and water matrices, *Journal of Chromatography A, 1153 (2007) 130–144*
17. Martin Harper, Sorbent trapping of volatile organic compounds from air, *Journal of Chromatography A, 885 (2000) 129–151*
18. Anastasia D. Nikolaou, Spyros K. Golfinopoulos, Maria N. Kostopoulou, George A. Kolokythas, Themistokles D. Lekkas, Determination of volatile organic compounds in surface waters and treated wastewater in Greece, *Water Research 36 (2002) 2883–2890*
19. Claudia Witschi, Erik Doelker, Residual solvent in pharmaceutical products: acceptable limits, influences on physicochemical properties, analytical methods and documented values, European Journal of Pharamceutics and Biopharmaceutics 43 (1997) 215-242
20. Jo Dewulf, Herman Van Langenhove, Anthropogenic volatile organic compounds in ambient air and natural waters: a review on recent developments of analytical methodology, performance and interpretation of field measurements, *Journal of Chromatography A, 843 (1999) 163–177*
21. Method EPA 8015D, Non-halogenated organics using GC-FID, *Revision 4 June 2003*
22. Method 8260C, Volatile Organic Compunds by gas chromatography / Mass Spectrometry

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