Navven Kumar M. et al. / Vol 4 / Issue 8 / 2015 / 456-463.

International Journal of Pharmaceutical Research & Analysis

e-ISSN: 2249 – 7781
Print ISSN: 2249 – 779X

www.ijpra.com

GREEN ANALYTICAL CHEMISTRY

M. Naveen Kumar*, G.UshaSree, A. Ajitha, V. Uma MaheshwarRao

CMR College of Pharmacy, Kandlakoya, Medchal, Telangana, India.

ABSTRACT

Analytical methods are developing rapidly, and it is considered to be a small-scale activity, but this is not always true in the case of controlling and monitoring laboratories whose number of runs performed is high. This makes an analytical laboratory comparable with the fine chemicals or pharmaceutical industry. Hence new analytical methodologies are being developed, according to green chemistry standards and these chemical processes are evaluated for their effects on the environment. Furthermore, most of these techniques can be automated and quite easily coupled with "green" methods. Introducing these techniques to everyday practice intolaboratories is an important step in diminishing the negativeeffects of analytical chemistry on the environment.

Keywords: Green Chemistry, Supercritical Fluid Extraction, Solid Phase Extraction.

INTRODUCTION

Great improvement in standard and comfort of living of wide fractions of populations, especially in developed countries, and the drastic increase in the total population of our globe have been observed since the last century. However, they were accompanied by environmental pollution, which has had large negative impact on the environment as a whole and human health in particular. A lot should and has been done to counteract environment damage by reducing production and use of chemicals. The consciousness, interest and activities in the field had reached such level that a new term "green chemistry" was introduced. It was first used by Anastas in a special program launched by the US EPA and has become now increasingly popular. Green chemistry is an approach to synthesis, processing and use of chemicals in environmentally friendly way. It is the 12 Principles of Green Chemistry which must be satisfied to make chemical products, processes and their application green [1].

The activities of chemists and chemical engineers, both in industry and in laboratories, can adversely affectthe quality of the natural environment. Growing publicconcern over protecting our environment obligates chemiststo change their attitude towards activities so that theywill be conducted in an environmentally friendly manner. Even modern analytical techniques are often not sufficiently sensitive and selective to analytes to assure reliable and meaningful data. Therefore, the application of standard instruments and procedures must often be preceded by extraction of analytes of interest from the large original sample and transfer them to a much smaller volume of a medium compatible with the applied technique. The process frequently results in generation of a large amount of waste, may in factbe the source of emission of a great amount of pollutantsthat negatively influence the environment. The production of reagents and solvents which are used for the purpose could also be a source of pollution. To combat the problems new sample preparation techniques have been developed and research has been conducted on miniaturization of sample preparation and analytical measuring instruments. The analytical procedure can be made greener at any of the steps of chemical analysis. Therefore, itis necessary to introduce the rules of green chemistry intochemical laboratories on a large scale [2].

Green chemistry

Green Chemistry is the utilisation of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products [3].

Corresponding Author:-M. Naveen Kumar Email:- mallepallynaveenkumar@gmail.com

Green chemistry is about

- Waste Minimisation at Source
- Use of Catalysts in place of Reagents
- Using Non-Toxic Reagents
- Use of Renewable Resources
- Improved Atom Efficiency
- Use of Solvent Free or Recyclable Environmentally Benign Solvent systems [3].

The 12 Principles of Green Chemistry

1. Prevention

It is better to prevent waste than to treat or clean up waste after it has been created.

2. Atom Economy

Synthetic methods should be designed to maximise the incorporation of all materials used in the process into the final product.

3. Less Hazardous Chemical Synthesis

Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to people or the environment.

4. Designing Safer Chemicals

Chemical products should be designed to effect their desired function while minimising their toxicity.

5. Safer Solvents and Auxiliaries

The use of auxiliary substances (e.g., solvents or separation agents) should be made unnecessary whenever possible and innocuous when used.

6. Design for Energy Efficiency

Energy requirements of chemical processes should be recognised for their environmental and economic impacts and should be minimised. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7. Use of Renewable Feedstocks

A raw material should be renewable rather than depleting whenever required.

8. Reduce Derivatives

Unnecessary derivatization (use of blocking groups, protection/de-protection, and temporary modification of physical/chemical processes) should be minimised or avoided if possible, because such steps require additional reagents and can generate waste.

9. Catalysis

Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for Degradation

Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

11. Real-time Analysis for Pollution Prevention

Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.

12. Inherently Safer Chemistry for Accident Prevention

Substances and the form of a substance used in a chemical process should be chosen to minimise the potential for chemical accidents, including releases, explosions, and fires [3].

Green analytical chemistry

Analytical chemistry dealing with analytical methods, techniques, procedures and lab routines which are increasingly environmentally friendly is termed Green Analytical Chemistry[1].

Considering the Twelve Principles of Green Chemistry it is easy to indicate the directions that may decide about the "green" character of analytical chemistry [2].

The following issues should be treated as priorities

– eliminating or minimizing the use of chemical reagents, particularly organic solvents, from analytical methods.

– eliminating from analytical procedures chemicals with high toxicity and ecotoxicity.

– reducing steps that demand much labor and energy, in particular analytical methods (per single analyte).

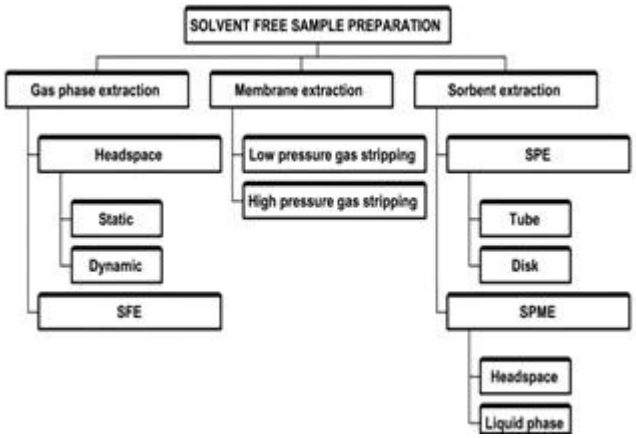
– reducing the impact of chemicals on human health [2].

Types of direct analytical techniques

- Potentiometric techniques (ion-selective electrodes ISE).
- Flameless atomic absorption spectrometry with (in a graphite cuvette).
- Inductively coupled plasma emission spectrometry (ICP).
- Neutron activation analysis (NAA).
- X-ray fluorescence spectrometry (XRF).
- Surface analysis techniques (AES, ESCA, SIMS, ISS).
- Immunoassay (IMA) [4].

Classification of solvent-free sample preparation methods

Scheme 1. Techniques for the solvent –free preparation of samples for analysis



Classification of solvent-free sample preparation methods

Headspace analysis

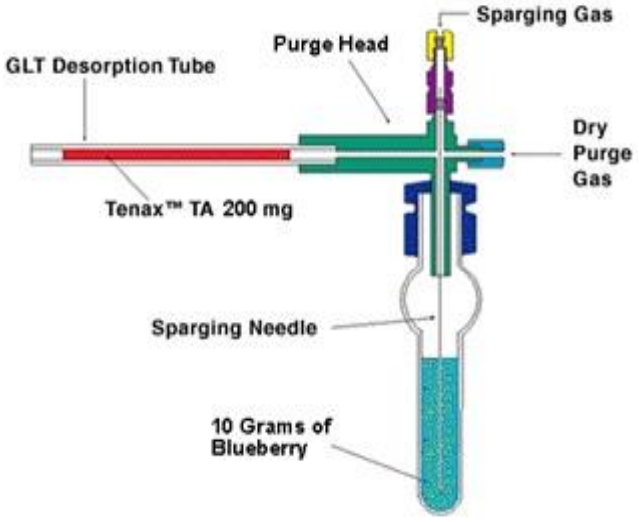
In HS analysis, the volatiles in the sample material are equilibrated with a gas phase above the sample in a closed vial. After a predetermined equilibration time, part of the gas phase is (automatically) withdrawn from the vessel, and injected into a GC system. For compounds which, because of low distribution constants, largely remain in the liquid or solid matrix, an obvious way to enhance the analyte concentration in the gas phase is to increase their vapour pressure by increasing the equilibration temperature or to decrease the activity coefficient by, e.g., increasing the ionic strength of the solution ('salting out'). In liquids, analyte diffusion generally is fast enough for equilibrium to be reached in a short time and many HS systems have stirring facilities to aid this. In (semi)solids, however, diffusion is often very slow and procedures such as grinding of the sample are used to speed up the analysis. After equilibrium has been established in the carefully thermostated vial, the gas phase is sampled using a syringe for manual procedures or automatically using commercially available pneumatic headspace analysers. Pneumatic sampling ensures that both the pressure and volume of the headspace sampled are identical for all samples and standards. A constant pressure is obtained by pressurizing the headspace vials with an inert gas to a pressure at least equal to the column inlet pressure. The sample is then either expanded directly into the column or to a sample loop of a thermostated gas-sampling valve. Instead of first filling a loop, a pressurized headspace gas can also be expanded directly into the GC column by using a so-called balanced sampling system [5].

Another procedure to collect the static headspace from a sample is the use of a sorbent. The adsorbent is allowed to stay in the headspace for a specific period of time and at a constant temperature. After equilibrium has been reached, the solid sorbent is transferred to a thermal desorber. In the past this procedure was often performed using small paper bags ('teabags') filled with Tenax or another polymer sorbent. Today, an SPME fibre is typically used (HS-SPME). In this technique, the distribution is between the fibre and the matrix. Consequently, even though raising the temperature increases the analyte concentration in the headspace, it reduces the deposition on the fibre because the vapour concentration of the analyte increases above the sample, but also above the fibre. HS-SPME can therefore give a selectivity which markedly differs from that of HS analysis: HS will favour the volatile analytes, but HS-SPME the less volatile compounds [5].

Supercritical Fluid Extraction

One area that stimulated an interest in enhanced fluid extractions was super-critical fluid extraction (SFE). This is a long established method, which has been used industrially for many years. Almost all SFE employs carbondioxide (critical point, 30.9C, 73.8 bar) as the supercritical fluid: it is an almost ideal solvent since it combines low viscosity and high analyte diffusivities with a high volatility (which makes analyte recovery very simple and provides solvent-free concentrates), and is inexpensive and environmentally friendly. An important drawback of CO2 is its non-polar character. In order to widen the application range of the technique to include more polar analytes, the preferred route is to employ polar modifiers such as methanol, ethanol, acetone and acetonitrile (1–10% addition, preferably by means of a separate modifier pump). In addition to a modifier pump, the basic components of an SFE system are supply of high purity carbondioxide; a CO2 pump; an oven for the extraction vessel; a pressure outlet or restrictor; and a suitable collection vessel for recovery of the extracted analytes [5].

Scheme 2. A Schematic of diagram of Head space analysis

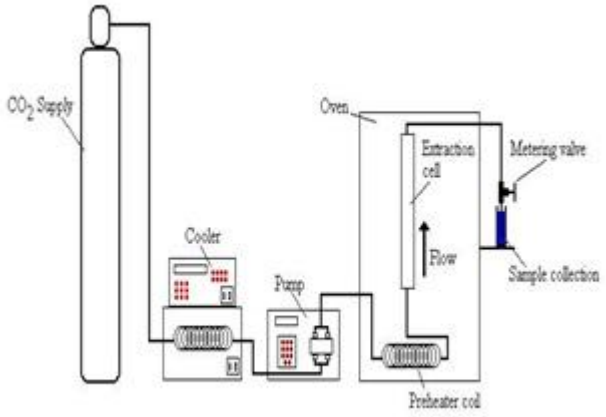


Sample collection can be performed by purging the extract through a solvent or over a suitable adsorbent, such as, Florisil. SFE comprises two integrated parts, extraction of the analyte from the sample matrix and subsequent collection or trapping of the analytes [5].

There are three main collection modes: (1) collection in a vessel containing solvent; (2) trapping on a cartridge packed with an adsorbing or inert solid-phase material and (3) collection in a device that is connected on-line with the chromatographic system. However, sample size should be limited since co-extracted fat or water may easily contaminate the interface used and or ruin the analytical column. For the rest, it is good to add that all three types of collection require careful optimization, with solvent collection probably being the simplest system to use and the easiest to optimize, and solid-phase trapping offering selectivity by the two-step trapping/elution procedure. On-line collection provides the best sensitivity

because the entire extract is introduced into the GC system [5].

Scheme 3.A schematic of a basic SFE system and back pressure regulator (with controller unit)



Membrane Extraction

Separation by means of a membrane can be achieved in many ways and very generally, a membrane can be defined as a selective barrier between two phases. When a driving force is applied across a membrane, transport of matter occurs from the donor to the acceptor phase,giving the so-called flux. Separation is achieved when some species are transported to a larger extent than others and, in the ideal case, components of interest are transferred quantitatively, while all other sample components remain in the donor phase [5].

Membrane separation processes can be classified by means of the driving forces involved. The most important ones are differences of (1) concentration, which cause a molecular flux , (2) electric potential, which cause an electrical flux (transport of charge) and pressure, which cause a volume flux (transport of bulk liquid or gas). Very often, more than one driving force is present in a membrane separation process. A wide variety of membrane materials can be used. In many cases, a membrane is a porous network of a synthetic polymer, such as polypropylene, polysulphone or a cellulose derivative. Separation is based only on size exclusion: sufficiently small molecules can permeate through the pores but larger ones cannot. More selectivity can be obtained with, e.g., ion-exchange membranes, which have positively or negatively charged groups covalently attached to the polymeric membrane material. Separation is now based on both size and charge differences of the various solutes [5].
Non-porous membranes are a rather different class: they consist of a liquid or polymer film, into which a molecule must actually dissolve in order to be able to pass through. For a particular compound, the efficiency of membrane transport now largely depends on its partition coefficients between the different parts of the membrane separation system. Only compounds which are easily extracted from the donor phase into the membrane and in addition, easily extracted from the membrane into the acceptor phase will be transported. Separation is therefore based on the same principle as in LLE with a subsequent back-extraction and analytes with different physicochemical properties will be extracted to a different extent even if they are of equal size [5].

Four membrane separation techniques are frequently used for sample preparation. Three of these—dialysis(concentration-driven) , electrodialysis (electrically driven) and filtration (pressure-driven)—utilize porous membranes and are combined (mainly) with LC. One technique, so called membrane extraction, uses non-porous membranes and is combined with LC as well as GC. The most frequently used membrane-extraction system, referred to as supported liquid membrane (SLM), consists of a porous membrane support impregnated with a water-immiscible organic solvent, which is present in the membrane pores [5].

In another approach, non-porous silicone rubber is used as the membrane material. In both cases, the membrane separates two aqueous phases and the sample pH (donor channel) is adjusted to ensure that the analytes of interest are not charged and are easily extracted into the membrane liquid or the silicone polymer film.

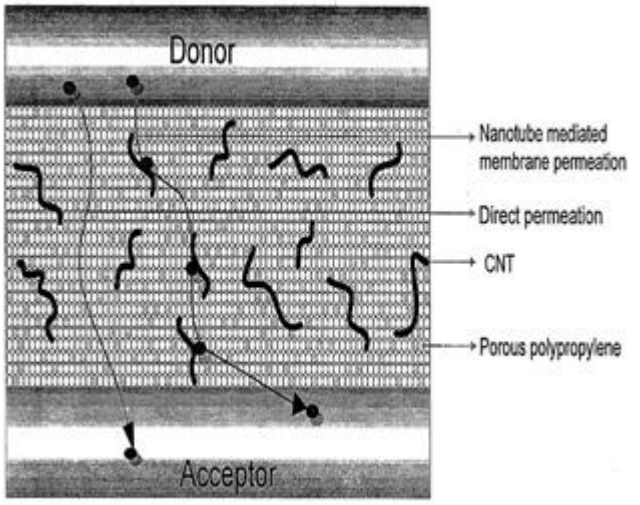
The acceptor phase has the proper pH to effect ionization of the analytes immediately after their passing the membrane to prevent back-extraction. With the silicone membranes one can also add an organic solvent to the acceptor phase to improve the trapping of neutral compounds. The third mode of membrane extraction uses a porous membrane with an organic solvent, both in the membrane pores and in the acceptor channel. Both flat-sheet an hollow-fibre membrane units can be applied. With this technique, micro porous membrane LLE (MMLLE), larger extraction surfaces can be achieved with the hollow fibres , which leads to improved extraction efficiency [5].

Counter-current donor/acceptor solvent flow is usually applied in order to create optimum conditions. MMLLE differs from the other two in that it can be compared to a single LLE step rather than to LLE plus a back-extraction. A common characteristic of all three techniques is that selectivity is obtained because sample components which do not readily dissolve in the membrane liquid, are retained in the donor channel. When using a stagnant acceptor phase and a flowing donor phase (the most common way of membrane extraction), the donor phase flow-rate will have a distinct influence on the membrane-extraction performance. If low detection limits are required and there are no sample-volume limitations (e.g., with natural waters), the best option is to use a large sample and apply a relatively high donor flow-rate of, often, 1–2 mL min. If sample volume is a limiting factor, such as for plasma, the sample is either kept stagnant in the

donor channel or pumped at a low flow-rate of typically 25–50lL min [5].

Also for membrane extractions, there are some practical limitations and aspects worth taking into account. A problem is the incomplete transfer of analytes from the membrane to the acceptor phase during the sample preparation process. This leads to a decrease in the recovery and, more seriously, to carry-over effects for sequential analyses. Thorough rinsing of the acceptor channel is therefore essential. In general, if analytes are easily extracted into the membrane, they also show large carry over effects obviously because they have a high affinity for the membrane material and are not readily released into the acceptor phase. Since for MMLLE there is no distinction between the membrane solvent and the acceptor phase, there are no problems of slow mass transfer to the acceptor phase or serious carry-over effects with this technique. Leakage of the membrane liquid adversely affects the extraction performance and should be avoided as much as possible. Membranes impregnated with non-polar solvents which are insoluble in water, are generally stable for several weeks without any regeneration [5].

Scheme 4.Schematic of diagram of membrane extraction



Solid-Phase Extraction

SPE was introduced for the pre-treatment of aqueous samples. Since that time, off-line, by means of SPE using pre columns or (disposable) cartridges has become a very popular probably the most popular column-switching technique in LC.SPE cartridges have dimensions of, typically, 10–20 mm length x 1–4.6 mm ID. In most instances the cartridges are packed with 10–30 lm sorbents such as C18- or C8-bonded silica or a styrene divinylbenzene (SDB) copolymer. These are essentially non-selective sorbents because for many applications the SPE step should primarily guarantee the enrichment of analytes covering a wide range of polarities, with the subsequent chromatographic separation (plus detection) step ensuring the proper recognition of the individual compounds. Since separation-plus-detection is much more powerful in GC than in LC analysis, with the former technique the bonded silicas and the copolymer are virtually the only sorbents used in real-life applications [5].

Solid-Phase Micro-Extraction

In 1990, solid-phase micro-extraction (SPME) was introduced by Arthur and Pawliszyn as an organic-solvent-free extraction technique. The theory and practice of the method have been examined in considerable detail and numerous applications have been reported and reviewed [5].

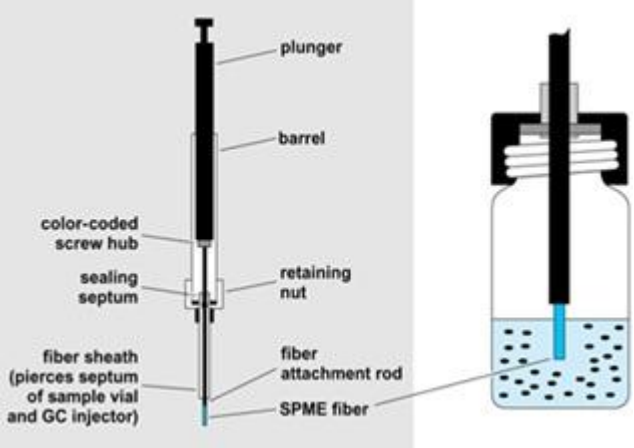
Basically, the technique enables the trace enrichment of analytes by the exposure of a fused-silica fibre coated with an appropriate sorbent layer, for a selected time, to a gas or liquid sample, with the subsequent (rapid) desorption of the target analytes by heating the exposed fibre in the injection port of a GC. A number of fibre coatings, which offer a range of analyte solubilities and porosities, are commercially available. These include the highly popular non-polar polydimethylsiloxane (PDMS) and more polar coatings such as PDMS divinylbenzene copolymers, polyacrylates and mixtures of carboxen (an inorganic adsorbent) and PDMS or divinylbenzene. Their mutually different physicochemical characteristics help to widen the application range of the technique. Fibre coatings are available in increasing thicknesses from 7–150lm, which increases the partitioning ratio of the target analytes and, hence, analyte detectability but also increases equilibration times.

The fibre is mounted in a syringe-like device for protection and ease of handling. The needle serves to conveniently pierce the septum of a sample vial or the GC injector. That is, during analyte extraction and desorption, the fibre is exposed but during transfer of the sample to the GC injector, it is inside the protective needle. Obviously, this is an elegant approach, and the fact that no solvent is required is a distinct advantage. On the other hand, it is a disadvantage that the fibres are rather fragile, even though they are shielded when out of the sample or injector; they can also be damaged by the buildup of in volatile material from the samples. [To improve the robustness of the technique, Lipinski introduced (automated) solid-phase dynamic extraction (SPDE) which uses needles prepared from stainless-steel capillary columns, with PDMS-coated inner walls].

In a typical SPME experiment, the coated fibre is exposed directly immersed in, or to the headspace of, a small volume of liquid or sample extract, usually some 2–5 mL. The analytes partition into the stationary phase until plateau conditions are reached, which typically takes 2–60 min. The process can be aided by salting-out (addition of, e.g.,25% NaCl) and/or pH adjustment, sample agitation (to

speed up analyte transport from the bulk of the solution to the vicinity of the fibre) and heating [5].

Scheme 5.Asection view of SPME holder and fibre assembly



Ionic liquids

ILs are salts with amelting point close or below room temperature. They form liquids composed ofions. This gives these materials, when used as solvents, the potential to behave very differently fromconventional molecular liquids. Their physical properties are very promising for green chemistryapplications: they are nonvolatile liquids and good solvents for many organic and inorganic materials.One of the advantages of ILs is thermal robustness. This means that the wide thermal operating range(typically, –40 to 200 °C) is possible that enables a wide range of kinetic control for reactions that proceedin ILs [6].

The most popular ILs are 1-alkyl-3-methyl imidazolium salts and 1-alkyl pyridinium salts with a multiple selection of anions. The search for applications is intensifying in each area of analytical chemistry electrochemistry, chromatography, and electrophoresis, even mass spectrometry. The basis for this activity is an easy preparation of salts with different ion constituents. This ability might best be described as the "chemical tunability" of ILs—a class of solvents with members possessing similar physical properties but different chemical behavior. ILs can be applied not only in the existing methods whose sensitivity and selectivity of analysis need to be improved, but their different behavior and properties can offer original solutions in chemical analysis as well[6].

ILs have good solvating properties, which together with a large range of spectral transparency make them suitable solvents for spectroscopic measurements of a wide range of species including organic, inorganic, and organometallic compounds. Notably, a variety of transition-metal complexes, which are unstable in other media, may be studied in room-temperature ILs. The use of room temperature ILs as solvents for UV, visible, and IR spectroscopy for highly charged complex ions with high or low-oxidation states like [MXn]y- complexes (M = transition metal; X = Cl, Br) circumvents the problems of solvation and solvolysis and permits reliable solution spectra to be recorded for these species. Spectroscopic measurements of solvatochromic and fluorescent probe molecules in room temperature ILs provide insights into solvent intermolecular interactions, although interpretation of the different and generally non correlated "polarity" scales is sometimes ambiguous. It is demonstrated that task-specific ILs have advantages over common solvents used as separation media in an LLE process achieving high efficiencies and selectivities of separation[6].

ILs' main advantage over organic solvents for other applications in analytical chemistry is their low volatility, which makes ILs useful as solvents for working at high temperature as well (GC stationary phases). The task-specific ILs have a high thermal stability up to 260 °C, provide symmetrical peak shapes, and because of their different for anions and cations range of solvation-type interactions, exhibit dual-nature behavior of selectivity . It seems that ILs are not very good media for liquid separation, and in liquid chromatography and CE applications they are used as specific additives. It was found in that ILs of the imidazoliumtetrafluoroborate class, added to mobile phases at a concentration of 0.5–1.5 % (v/v), blocked silanols and provided excellent chromatographic separations of strongly basic drugs which were otherwise not eluted, even with neat acetonitrile as a mobile phase. In many cases, salts, which are liquid at room temperature, show a better solubility in organic solvents and can be used in nonaqueous CZE as ionic additives for adjustment of analyte mobility and separation. The separation of different analytes in organic solvents is achieved because they become charged in the presence of ILs in the separation media. The low volatility of ILs makes them useful as solvent working in a high vacuum, and together with their more amorphous solid analogs they merit further study as MALDI matrixes. These ionic matrix systems allow a homogenous sample preparation with a thin IL layer having negligible vapor pressure [6].

The vacuum-stable, liquid consistency of IL matrix sample preparations considerably enhanced MALDI-MS analysis in terms of shot-to-shot reproducibility, and this leads to a facilitated qualitative and quantitative measurement of analytes compared with classical solid matrixes .

Good electrolytes should have high conductivity, large electrochemical windows, excellent thermal and chemical stability, and negligible evaporation. Using an IL as an electrolyte medium, it is possible to achieve a wider range of operational temperatures and conditions, relative to other conventional electrolytic media, and make them promising materials in various electrochemical devices,

such as batteries, fuel cells, sensors, and electrochromic windows [6].

The combination of ILs with supercritical carbon dioxide (scCO2) as an extractant offers a potential for a chemical reaction and downstream separation in one system. Spectroscopic studies can offer reliable data on the properties of the media. The authors study of the solvent properties of mixtures of 1-butyl-3-methyl imidazolium hexafluorophosphate and CO2 as functions of temperature (35–50 °C) and pressure of CO2 (0–230 bar). The results are consistent with a picture of local enhancement of an IL around a chromophore, maintaining solvent strength even at fairly high loadings of CO2, whereas the microviscosity in the vicinity of the solute is dramatically reduced, leading to enhanced mass transport and facilitated separation. They can be used together with organic cosolvents which "solvate" the constituent ions of the IL, resulting in a decrease in the aggregation of these ions (lower viscosity and higher conductivity) [6].

Lack of understanding of solvent/materials properties with regard to the structural features of the ILs (effect of anion choice and cation substitution) is substantial and a very promising area of study. ILs are commercially available, and intensive studies are underway in every area of chemistry to find a proper niche for them [6].

Micronization in separation methods

Micronization is an important approach to minimize the waste generated and is essential for analysis when the amount of sample available is very small (less than microliters).The key to a rapid and efficient synthesis is not only the parallel arrangement of reactions, but simple workup procedures so as to circumvent time-consuming and laborious purification steps [6].

The similar reasoning applies even more to microfluidics in the case of which the amount of eluent consumed is even lower than in CZE. Miniaturized total analysis systems (μTAS) were first proposed as a novel concept for chemical sensing in 1990 , developing the field of microfluidics and leading to the vision of lab-on-a-chip. μTAS integrates all steps required in chemical analysis—sampling, pre-processing, and measurement—into a single device via miniaturization, resulting in an improved selectivity and detection limit compared to conventional sensors [6].

Also, the dramatic downscaling and integration of chemical assays hold a considerable promise for a faster and simpler onsite monitoring of priority pollutants and make these analytical microsystems particularly attractive as"green analytical chemistry" screening tools. The amount of waste generated is reduced by ca. 4–5 orders of magnitude, in comparison. A significant amount of research has been devoted to the development of microfluidics technology and applications of μTAS devices over the past decade . Common analytical assays, including polymerase chain reaction (PCR), DNA analyses and sequencing, protein separations, immunoassay, and intra- and inter-cellular analysis, have been reduced in size and fabricated in a centimeter-scale chip . Although there have been many successes, an important hurdle that still needs to be cleared is the connection between the microcomponents of a device and the macro-environment of the world. This part of the device is often referred to as the macro-to-micro interface , interconnect , or world-to-chip interface . The difficulty results from the fact that samples and reagents are typically transferred in quantities of microliters to milliliters (or even liters) while microfluidic devices consume only nanoliters or picoliters of samples/reagents due to the size of reaction chambers and channels, which typically have dimensions of the order of microns. Although designed lab-on-chip applications, these world-to-chip designs might be relevant in designs of similar interfaces for common CZE as well. The aim of such designs could well aim at achieving a computerized on-line sampling of small sample volumes without incurring complications of microfabrication. The first approach was similar to the "cross" injection device commonly used in lab-on-chip devices where sample and separation channels are located perpendicularly on a chip. However, instead of an electrokinetic loading, in this work the sample is loaded into a capillary by pressure pulse [6]. This sampling technique has been used for microfabricated systems by Lin et al.. In the second approach, the sample is delivered as droplets (10 μL volume) into a buffer situated in a pipette tip. The falling droplet sampler was implemented for hyphenating flow injection analysis (FIA) to CZE. Recently falling droplet sampling was adopted in the FIA-CZE system to avoid deterioration of separation due to hydrodynamic pressure created in the inlet, especially with higher flow rates in the FI system . In this falling-drop design, a constant liquid head, equal to that at the capillary outlet, is maintained and the Poiseuille flow is avoided. In the design proposed in , the construction of the falling droplet sampler was further simplified by rejecting a specially designed FI-CZE interface body. The liquid was kept in the pipette tip by surface tension and if a new portion of liquid is delivered, it displaces an old portion that flows into a waste [6].

Green methodology in analytical chemistry

- Reducing consumption of reagents and solvents- Solvent free sample preparations , use of green media and direct analytical techniques.
- Saving energy- Shorten analysis time enhancement of efficiency of some processes.
- Reducing gas and vapour emissions -Hermetization analytical operations and
solvent free sample preparations.
- Reducing amounts of waste and effluents-Direct techniques, recycling of media, solvent free sample preparations.

• Promote human health-By use of green solvents and reagents [4].

Pharmaceutical applications

• It has shown that by adjusting two of the GC headspace parameters (i.e., vial volume and equilibriation time), the consumption of sample and analysis time can be reduced. Finally, by trying different diluents (i.e., DMF versus DMSO for allylamine) and multicomponent diluents, containing a small amount of aqueous, the analysis of difficult analytes may be improved by enhanced sensitivity [7].

• In the case of triethylamine, the signal increased by 60% by using a diluent 80:20 ratio of DMSO:water instead of just DMSO. For allylamine, however, no combination of solvents yielded a signal higher than that with just using DMSO.

• Supercritical Fluids have been mostly developed for natural products extraction/fractionation, both for food and pharmaceutical products. Supercritical Fluid technology is widespread in the pharmaceutical industry, for extraction of active compounds from vegetal sources (phytopharma-/nutra-ceuticals) [8].

• SPME methods have been developed to extract of drugs from various biological samples, including urine, serum, plasma, whole blood, saliva and hair. The number of publications reporting pharmaceutical and biomedical applications of SPME has increased exponentially. Low volatility drugs and metabolites in plasma may be limited to those with high therapeutic concentrations, in the range of 1 to 100 µg/mL. In particular, hair analysis is frequently used for the long-term monitoring of drug and alcohol users [9].

• Non-porous and microporous membranes are versatile structures that can be used for the extraction and concentration of a wide range of compounds, such as, VOCs, SVOCs, organic acids, ions and metals.

• Polar and non-polar VOCS, e.g. benzene, toluene, chlorobenzene, methanol, acetone, methylene chloride, o-nitrotoluene. Polar and non-polar SVOCs, e.g.PAHs, acids, PCBs, pesticides, drugs and their metabolites, anesthetics [10].

CONCLUSION

Analytical methods are developing rapidly, and it is considered to be a small-scale activity, but this is not always true in the case of controlling and monitoring laboratories whose number of runs performed is high. This makes an analytical laboratory comparable with the fine chemicals or pharmaceutical industry. Hence new analytical methodologies are being developed ,according to green chemistry standards and these chemical processes are evaluated for their effects on the environment. Furthermore, most of these techniques can be automated and quite easily coupled with "green" methods. Introducing these techniques to everyday practice into laboratories is an important step in diminishing the negative effects of analytical chemistry on the environment.

REFERENCES

1. Zygmunt B, Banel A, Wasielewska M. Green Analytical Chemistry in Determination of Volatile Fatty Acids in Wastewater - Proceedings,2nd ed, 2011.
2. Curylo J, Wardencki W and Namiesnik J. *Green aspects of sample preparation – a need for solvent reduction. Pol. J. Environ. Stud.*, 16, 2007, 5–16.
3. Wardencki W, Cury O, Namieœnik J. Green Chemistry — Current and Future Issues-a review. *Journal of Environmental Studies*, 14(4), 2005, 389-395.
4. Jacek N. *Green analytical chemistry*. Department of *Analytical Chemistry*. Faculty of *Chemistry*. Gdansk University of Ekopole, 2010.
5. Sjaak de K, Hans-Gerd J, Udo A. Th. Brinkman. Modern Methods of Sample Preparation for GC Analysis. 69, 2009, S33-S78.
6. Mihkel K and Mihkel K. *Application of the principles of green chemistry in analytical chemistry,* Institute of Chemistry, Tallinn University, 78(11), 2006, 1993–2002.
7. Laila K, Hong MC. Experimental Considerations in Headspace Gas Chromatography.*Pharmaceutical Technology*, 34(5), 2010, 76-79.
8. Michel Perrut. Pharmaceutical applications of Supercritical Fluids. *Invited lecture at the 8th Meeting on Supercritical Fluids (Bordeaux)*, 2002.
9. Hiroyuki K. Recent Advances in Solid-Phase Microextraction and Related Techniques for Pharmaceutical and Biomedical Analysis. *Current Pharmaceutical Analysis*, 1, 2005, 65-68.
10. Lidietta G and Enrico D. Biocatalytic membrane reactors: applications and perspectives.*TIBTECH*, 18, 2000.