

Editorial

# Pharmaceutical Analysis from a Green Perspective

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Green approach in chemical processes is a recent issue arising from the scientists' concern for human health, environment protection and sustainability. According to Paul Anastas, the term "Green Chemistry" can be defined as "*the design of chemical products and processes that are more environmentally benign*", which fulfill requirements for the reduction of negative health and environmental impacts.

Some of the Green Chemistry principles can directly be adapted to the analytical field, whilst others are mostly related to chemical synthesis.

## General Aspects of Green Analytical Chemistry

The use of less hazardous, green solvents, easily degraded reagents and renewable sources constitute the core of green chemical analysis demands, but they are not the only ones. Recent advances in technology have been implemented in the analytical process.

Miniaturization along with reagent replacement was the first attempt in green analytical chemistry (GAC). These comply with the first declaration in 1994 about green analytical chemistry by M.de la Guardia and J.Ruzicka. Since then great progress has been accomplished to this direction.

Jacek Namiesnik has proposed the twelve principles of Green Analytical Chemistry that include:

1. Direct analysis avoiding sample preparation.
2. Reduced sample size.
3. In situ analysis.
4. Use of integrated processes in order to save energy and prevent spending high amounts of reagents.
5. Automation and miniaturization.
6. Less or no derivatization.
7. Reduced waste.
8. Developments of methods for the simultaneous analysis of multiple analyses.
9. Reduction of energy consumption.
10. Use of renewable sources.

11. Replacement of toxic reagents or reduction of their use.
12. Great concern for the safety of analytical operator.

These principles were subsequently summarized by the same author in four strategies as follows: 1. Elimination or significant reduction of solvent and reagents consumption. 2. Reduction in wastes, 3. Elimination of toxic reagents' usage, and 4. Reduction of labor and energy consumption during analytical processes.

## Green Analytical Techniques

Concerning the instrumentation, obviously some analytical techniques are considered to be greener than others, as for example is Flow Injection Analysis (FIA) compared to the conventional High Performance Liquid Chromatography (HPLC). Other techniques like Sequential Injection Analysis (SIA), Capillary Electrophoresis (CE), or Capillary Electro chromatography (CEC) have been also suggested as the greener approach in analytical chemistry replacing the organic solvent consuming analytical techniques.

Miniaturization of chromatographic equipment required pumps of new optimized technology. Thus Micro, Nano, Capillary HPLC or Ultra high performance liquid chromatography are the green version of the "old fashioned" HPLC.

Further technological advances like in-field direct analysis of untreated samples, the use of sensors, or solvent-less techniques were implemented in analytical methodologies according to what green chemistry dictates.

Moreover the impact of chemometrics in the green approach, for experimental design and optimization is undoubtedly significant.

Green strategies can be involved in both sample preparation and analysis steps.

Integrated approaches on microfluid platforms, e.g. lab-on-a chip concept, new automated sampling strategies like dried blood spot (DBS) sampling in therapeutic drug monitoring, modern sample preparation techniques, like microwave assisted solvent extraction (MASE), Solid Phase Micro extraction (SPME), Supercritical Fluid Extraction (SFE), Single Drop Micro Extraction, (SDME) and others are very promising in reducing solvent consumption. New materials of nanostructures, such as grapheme, carbon nanotubes, biomaterials, immune-affinity materials can promise greener approaches, in the field of sample preparation.

Additionally the replacement of solvents in chromatographic techniques by supercritical fluids, ionic liquids (not an inexpensive choice though), non-volatile organic solvents, water under superheated conditions, renewable solvents, etc, are the modern green approach concerning eluents and mobile phases.

The two most commonly used organic solvents in HPLC are acetonitrile and methanol. The former is toxic and as waste has to be detoxified through special chemical treatment of high cost. The latter

is also toxic to humans and causes adverse effects on the environment. Their replacement renders separation methods greener.

## Green Pharmaceutical Analysis

Pharmaceutical analysis is fundamental in the pharmaceutical industry.

In pharmaceutical manufacturing, analytical procedures are involved in various stages such as the quality control of raw materials and products, effluent monitoring, pharmacokinetics, pharmacological assays, clinical trials, stability indicating assays, impurities profiling etc.

Analysis of active pharmaceutical ingredients (APIs) and drug products, purity determination, enantiomeric separation, all rely on methodologies either newly developed or specified by regulatory agencies. Impurities that arise from various steps during synthesis, manufacture, storage or transportation must be characterized, and quantified. The great importance of their detection, structure elucidation and quantization is beyond any doubt, since they may cause various health problems. Their presence even in small quantities may give rise to safety, efficacy, purity, stability as well as quality issues. For this reason, regulatory authorities such as International Conference on Harmonization (ICH), the United States Food and Drug Administration (FDA), different Pharmacopoeias like British Pharmacopoeia, have set guidelines regarding their profiling in pharmaceutical formulations.

Guidelines set by regulatory agencies reassure the quality of pharmaceuticals all over the world. These provide the frame for validation of the analytical methods used.

All requirements related to Green Analytical Chemistry must be also fulfilled in pharmaceutical analysis, with special attention to the use of organic solvents which are extensively involved in almost all pharmaceutical processes e.g. drug synthesis, extraction, recrystallization, dissolution of solids and chromatographic analysis.

Some excellent contributions and thorough reviews with regards to the greener approach in pharmaceutical analysis are given as suggested further reading in the references' section.

## Concluding Remarks

It is important to develop green methods or make greener the already existing ones. As already mentioned most of the issues related to green analysis require reduction in sample number, reagents, energy, waste, risk and hazard. Downsizing in sample and reagents volume results also in the reduction of analysis time.

It is not always necessary to start from the beginning and build completely new analytical methods. By thinking greener all existing analytical methods can be modified so that they fulfill green chemistry requirements.

However, when trying to use green laboratory practice, the result might be a compromise between green demands and performance characteristics. And this is considered as a significant disadvantage. Despite the green analytical strategy, accuracy, precision, sensitivity and all other figures of merit must not be diminished. New

instrumentation can guarantee that new methodologies will still be reliable and effective.

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