

Green Analytical Methodologies

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Contents

1. Introduction	2695
1.1. Green Chemistry	2695
1.2. Green Analytical Chemistry	2695
2. Trends in Green Analytical Chemistry	2696
2.1. Greening Pretreatment	2697
2.1.1. Solvent Reduction and Replacement	2697
2.1.2. Solvent Elimination	2699
2.1.3. Derivatization of Molecules and Surfaces	2700
2.2. Greening Signal Acquisition	2700
2.2.1. Spectroscopy	2700
2.2.2. Electrochemistry	2700
2.2.3. Bioanalytical Chemistry	2700
2.3. Greening with Automation and Flow Techniques	2701
2.3.1. Flow Injection Analysis (FIA) and Sequential Flow Injection Analysis (SIA)	2701
2.3.2. Multicommutation	2701
2.4. Green by <i>in-Situ</i>	2701
3. NEMI and Greener Analytical Methods	2702
3.1. Background of NEMI	2702
3.2. Greenness Profiles of Greener Analytical Methods	2702
3.3. Application of Greenness Profiles	2703
3.4. Characteristics of Greener Analytical Methods in NEMI	2703
4. Conclusion	2706
5. Acknowledgments	2706
6. References	2706

1. Introduction

For over 10 years, the green chemistry movement has been promoting ways to reduce the risks of chemical use to humans and the environment.^{1,2} An important goal is to develop increasingly environmentally benign chemistries. A relatively underexamined area of green chemistry is analytical chemistry. However, analytical methods are not easily identified as being environmentally benign. Assessment requires careful examination of often complex analytical methodologies within the context of green chemistry. This article attempts to examine qualitatively the scope of green analytical chemistry with a survey of the recent analytical

literature to discern common green analytical chemistry themes while creating, and applying, a more quantitative approach to existing environmental methodologies. The authors set forth some basic characteristics, or “acceptance criteria”, to which analytical methods should conform in order to be called “green.” The application of these criteria, applied to over 800 methods in the National Environmental Methods Index (NEMI), the largest available database of environmental analytical methods, is discussed herein.

1.1. Green Chemistry

Simply stated, “Green Chemistry is the use of chemistry techniques and methodologies that reduce or eliminate the use or generation of feedstocks, products, byproducts, solvents, reagents, etc. that are hazardous to human health or the environment.”¹ Thus, an important goal of green chemistry is to reduce hazards associated with products and processes that are essential to the world economy and to sustain the high quality of living that we enjoy through chemistry. It seeks to achieve this goal by reducing or eliminating as much risk as possible associated with chemical processes. If chemical hazards can be reduced, then risks from using or being exposed to chemicals are also reduced. Hazards from chemicals go beyond toxicity (acute and chronic) to include carcinogenicity, mutagenicity, explosivity, flammability, and corrosivity as well as including environmental impacts such as atmospheric damage and global climate change.¹

The Twelve Principles of Green Chemistry provide a framework for scientists and engineers to use when designing new materials, products, processes, and systems.² The principles focus thinking in terms of sustainable design criteria and have proven to be the source of innovative solutions to a wide range of problems. Many, but not all, of these principles apply to green analytical chemistry. Those that are most relevant to, or most commonly encountered in, analytical chemistry are marked in bold and with asterisks in Table 1. For analytical methods, green chemistry means designing methods that reduce or eliminate the hazardous substances used in or generated by a method.

1.2. Green Analytical Chemistry

As Anastas alluded to, it is an unfortunate irony that environmental analytical methods often contribute to further environmental problems through the chemicals used in the analysis.¹ This is because many analytical procedures require hazardous chemicals as part of sample preservation, preparation, quality control, calibration, and equipment cleaning—effectively creating wastes in larger quantities and with

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Dr. Liz Gron earned her B.A. in chemistry at Colgate University and her Ph.D. in inorganic chemistry with Arthur B. Ellis at the University of Wisconsin—Madison, 1987. She was a postdoctoral fellow and an Industrial Research Liaison at the Department of Chemical Engineering, University of Delaware, before starting at Hendrix College in 1994. She is currently an Associate Professor of Chemistry at Hendrix College and has taught courses in general, analytical, and inorganic chemistry. Her research interests focus on the parallel development of green chemical reactions as well as the development of green pedagogical materials. Her chemical research investigates organic reactions in near-critical water as a solvent replacement technology while also exploiting the unique properties of extremely hot water to investigate underlying mechanistic interactions between the reactants and the solvent. Her educational materials development has focused on designing green experiments that teach analytical and environmental chemistry, particularly to introductory chemistry students. During her latest sabbatical, Professor Gron held the position of Visiting Assistant Professor of Chemical Engineering, Massachusetts Institute of Technology, while working as a Visiting Scientist with Professor Jefferson Tester.

greater toxicity than that of the original analyzed sample. For all of these reasons, green analytical chemistry is becoming a new and important subarea of green chemistry.



Dr. Jennifer L. Young is a senior program manager at the American Chemical Society Green Chemistry Institute (ACS GCI), where her work focuses on the development of research tools to aid chemists and engineers in implementing green chemistry and engineering. Prior to joining ACS GCI in 2004, she held an industrial polymer research position at DuPont in the Ink Jet business. Jennifer earned a Ph.D. in polymer/organic chemistry in 2000 from the University of North Carolina at Chapel Hill by researching polymerizations in supercritical carbon dioxide under the direction of Joseph DeSimone. Her B.S. degree in chemistry is from the University of Richmond. Jennifer has over 10 years of experience in green chemistry and has presented and published papers and book chapters on numerous green chemistry topics.

The goal of green analytical chemistry is to use analytical procedures that generate less hazardous waste and that are safer to use and more benign to the environment. This goal may be achieved by developing new analytical methodologies or, more often, simply modifying an old method to incorporate procedures that either use less hazardous chemicals or, at least, use lesser amounts of hazardous chemicals, if appropriate, safer chemical substitutions have not yet been discovered.

For a long time, analytical chemists have been environmentally sensitive but have rarely used the word “green”, making the green developments a little harder to discern in the literature. Since the first general reviews describing green analytical chemistry,^{1,3,4} more researchers are publishing on green or clean methodologies and using this terminology, with the trends in numbers of publications plotted in Figure 1. The scope of this review will provide a literature review of recent advances in green analytical chemistry as well as touch on some traditional methodologies that have always been environmentally benign, but perhaps not called green.

2. Trends in Green Analytical Chemistry

Analytical chemistry provides the data necessary to make decisions about human and environmental health. Fast, precise, and accurate results will always be the primary business of an analytical chemist; the new green challenge is to meet the informational needs of chemists, industry, and society while reducing the human and environmental impact of the analyses.

The natures of the analyte, the matrix, and the method of signal generation greatly influence the ease of creating a green analytical method. Analysis schemes that do not require pretreatment, use few reagents, or work with aqueous solvents have a greenness advantage. This covers several well-established techniques measuring aqueous inorganic ions, such as pH, ion chromatography, flame atomic absorption (FAA) spectroscopy, and graphite furnace atomic absorption (GFAA) spectroscopy. Elemental analysis in solid

Table 1. The Twelve Principles of Green Chemistry:² Asterisks and Bold Type Indicate the Principles Most Applicable to Analytical 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 maximize the incorporation of all materials used in the process into the final product.
3.	Less Hazardous Chemical Syntheses Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4.	Designing Safer Chemicals Chemical products should be designed to effect their desired function while minimizing their toxicity.
*5.	Safer Solvents and Auxiliaries The use of auxiliary substances (e.g., solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used.
*6.	Design for Energy Efficiency Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.
7.	Use of Renewable Feedstocks A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.
*8.	Reduce Derivatives Unnecessary derivatization (use of blocking groups, protection/deprotection, temporary modification of physical/chemical processes) should be minimized 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 minimize the potential for chemical accidents, including releases, explosions, and fires.

samples can be done readily without any sample preparation using X-ray fluorescence (XRF) spectrometry, where a sample is bombarded with high-energy X-rays, causing emission of a secondary X-ray photon, fluorescence, unique to the element. Very simple techniques for organics have a similar advantage of no sample pretreatment, such as gas chromatography (GC),⁵ attenuated total reflectance infrared (ATR) spectroscopy, and total organic carbon (TOC) analysis.

Analytical schemes include a myriad of steps, and most can be separated into two broad categories: the pretreatment steps (including digestion, extraction, drying, and concentration) and the signal acquisition step. Although an ideal green analysis would obviate preconcentration steps, the evolving understanding of the vanishingly low thresholds for the negative biological activity of many environmental contaminants suggests that analytical chemists will continue to need sample pretreatment as a tool to take measurements from dilute samples at, or below, the limit of detection.

A survey of the recent analytical literature illustrates that the path toward greening analytical methodologies includes incremental improvements in established methods as well as quantum leaps that completely rethink an analytical approach. Strategies used include changing or modifying the reagents and solvents, reducing chemicals used through automation and advanced flow techniques, miniaturization, and even eliminating sampling by measuring analytes *in-situ*, on-line, or in the field.

2.1. Greening Pretreatment

2.1.1. Solvent Reduction and Replacement

A rich variety of greener methods have been developed to extract and concentrate analytes. As a rule, accelerated solvent extraction (ASE), ultrasound extraction, microwave assisted extraction (MAE), supercritical fluid extraction (SFE), and membrane extraction reduce the use of organic solvents and speed extraction times compared to traditional liquid–liquid extractions. While ASE uses pressure and heat to speed extractions, up to 200 °C,⁶ the other methods use lower temperatures, allowing for easier handling of thermally fragile analytes and cleaner extractions. Ultrasonic and microwave extractions are relatively simple and inexpensive techniques for greening extractions, while SFE is more expensive due to the equipment and requires careful control of a wide variety of factors, making SFE more difficult to optimize and validate.

2.1.1.1. Ultrasound. Ultrasonic extraction uses high frequency acoustic waves to create microscopic bubbles in liquids. The collapse of the small bubbles produces small shock waves, cavitations, that are particularly well suited for breaking up or promoting the dissolution of solids. Ultrasonic extraction has been applied to a variety of organic extractions. These include the extraction of nicotine from pharmaceutical samples into heptane for GC analysis, which reduced the amount of solvent required by 5/6 compared to the conventional method,⁷ phthalates from cosmetics into

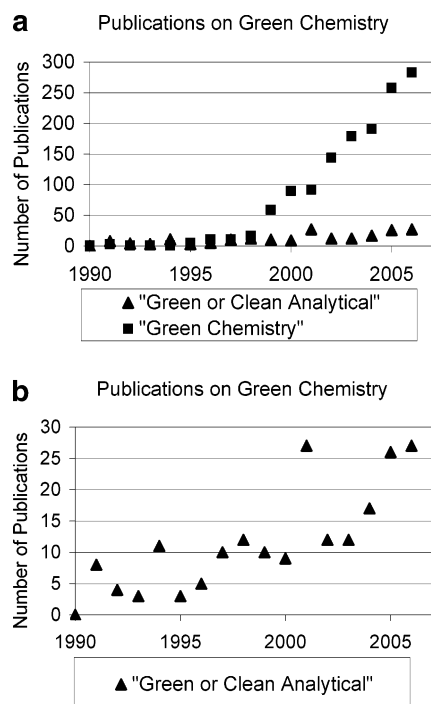


Figure 1. Number of publications resulting from an ISI Web of Science literature search for 1990–2006 for the keywords “green chemistry” (■) and the combination of “green anal*” or “clean anal*” or “green method*” (▲). Part a shows both keyword search results, and part b shows only the results for publications related to green/clean analytical methods.

ethanol/water for high performance liquid chromatography (HPLC),⁸ and UV filters from sunscreens into ethanol for liquid chromatography.⁹ Ultrasound has also been used for inorganic analytes, most recently to extract mercury into aqua regia from milk samples.¹⁰

2.1.1.2. Microwave-Assisted Extraction (MAE). Microwave-assisted extraction (MAE) has proven broadly applicable for extractions from difficult sample matrices, previously treated by time and solvent intensive Soxhlet extractions or hydrodistillations. Microwave extractions can be done in open or closed vessels, known as focused MAE and pressurized MAE, respectively. A recent review of the application of microwave techniques to environmental samples illustrates the wide range of matrices used, including the extraction of polycyclic aromatic hydrocarbons (PAH) from soil, polychlorobiphenyls (PCB) from coal, methylmercury from sediments, as well as trace metals and pesticide residues from plant materials.¹¹ The use of MAE has expanded with adaptations that include using focused MAE for Soxhlet extractions of thermally labile methylcarbamates¹² and acid herbicides¹³ from soil and using MAE to extract camphor or borneol from fresh herbs into water and then coupling to headspace solid-phase microextraction for re-concentration of the analytes.¹⁴ Microwave treatment can provide a solvent-free separation technique by providing heating and dry distillation for essential oils versus hydrodistillation.¹⁵ Figure 2 shows a solvent-free microwave extraction apparatus.

2.1.1.3. Supercritical Fluid Extraction (SFE) and Superheated Water Extraction (SWE). A variety of solvent technologies have been developed to replace non-renewable petroleum solvents. Once exotic, SFE has become a routine method for handling thermally sensitive analytes. Solvents that are heated and pressurized above their critical point

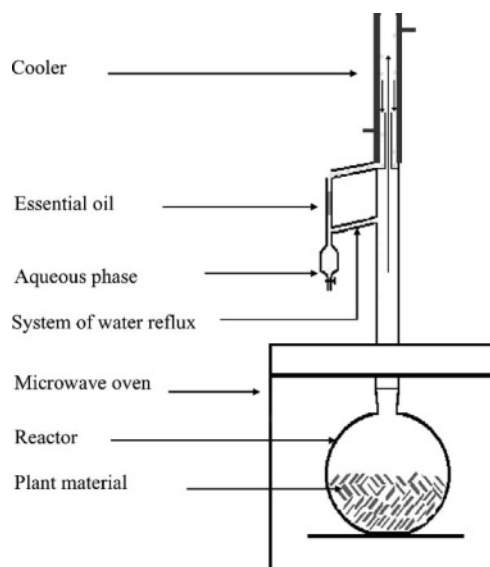


Figure 2. Solvent-free microwave extraction apparatus. Reprinted from *Journal of Chromatography A*, Vol. 1043, Lucchesi, M. E.; Chemat, F.; Smadja, J., Solvent-free microwave extraction of essential oil from aromatic herbs: comparison with conventional hydro-distillation, pp 323–327, Copyright 2004, with permission from Elsevier.

exhibit properties intermediate between those of liquids and gases, making them ideal for separations and extractions. Many SFEs are performed with carbon dioxide (SFE- CO_2), which has a readily accessible critical point (31.1 °C, 74.8 atm) along with being inflammable and nontoxic. The efficiency of SFEs is affected by the choice of extraction solvent as well as the extraction pressure, temperature, filler materials (mixed with the sample matrix), modifiers (cosolvents), and collection solvent.^{16,17} The challenge of SFE- CO_2 is the very low solubility of polar materials.¹⁸ The applicability of SFE- CO_2 has been broadened by the use of a modifier, primarily methanol,^{16,19} or the addition of chelates.²⁰

A polar alternative to SFE- CO_2 is superheated, subcritical, water extraction (SWE). SWE has the advantage of tunable polarity, since the dielectric constant of the pressurized water decreases dramatically with increasing temperature (100–373 °C) due to reduced H-bonding; however, these higher temperatures limit the method to relatively thermally robust analytes, for example organopesticides and triazine herbicides.^{21,22} High-temperature water is inflammable and nontoxic, but similarly to the SFE methods, many procedures use modifiers¹⁷ to optimize the extraction and the extraction yields a dilute aqueous sample which usually requires a subsequent concentration step. A truly unusual solvent system under development may provide the intermediate polarities that mixtures of supercritical fluids with cosolvents are trying to attain. These are gas-expanded liquids (GEL).²³ In this example, $\text{CO}_{2(g)}$ is added to a pressurized solvent, decreasing the dielectric constant and providing a truly tunable polarity at low temperatures.

2.1.1.4. Membranes. Membranes, selective barriers between phases, provide an alternative for green analyte isolation and preconcentration. There are two primary membrane techniques, filtration and extraction, which are thoroughly reviewed in a recent article.²⁴ Membrane filtration uses porous membranes to separate solution components based on size using a pressure difference between the donor and acceptor solutions as the driving force, whereas mem-

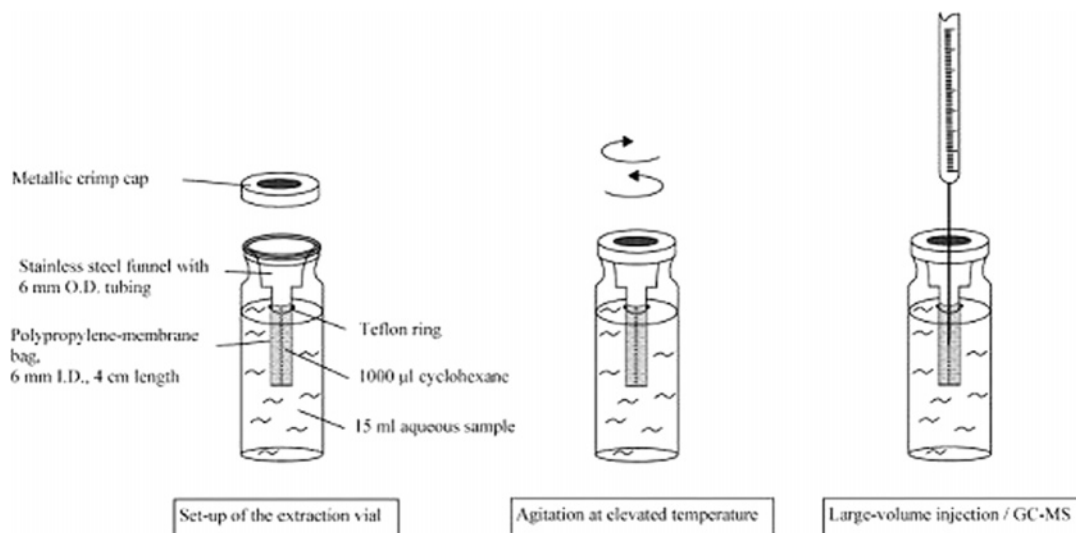


Figure 3. Experimental setup for using a membrane bag for extraction. Reprinted with permission from Hauser, B.; Schellin, M.; Popp, P. *Analytical Chemistry* **2004**, *76*, 6029. Copyright 2004 American Chemical Society.

brane extraction primarily exploits concentration gradients using nonporous membranes. Recent, novel adaptations of membranes include the application of microdialysis to environmental sampling^{25,26} and the use of a polypropylene membrane bag containing cyclohexane suspended into an aqueous sample (Figure 3) for the extraction of triazines and organochlorine and organophosphorus compounds.²⁷

2.1.1.5. Cloud Point Extraction. A less commonly used extraction is cloud point extraction (CPE), where the metals are extracted into micelles with a complexing agent in the presence of a surfactant. Above the critical micelle concentration (cmc), a separate phase is created. This is a simple means for quantifying metals spectroscopically.²⁸ This technique, illustrated in Figure 4, has recently been re-

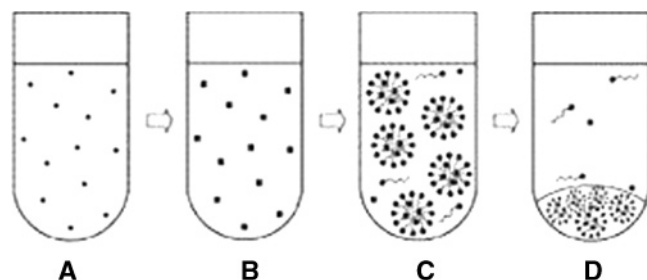


Figure 4. Schematic representation of a conventional CPE to metal preconcentration: (A) original solution with metals (circles) in low concentration; (B) metal chelates (squares) formed by addition of complexing reagent to the matrix solution; (C) addition of surfactant to the solution and trapping of metallic chelates into micellar cores; and (D) micellar phase segregation after heating and separation after centrifugation. Copyright 2005 from *Applied Spectroscopy Reviews* by Bezerra, M. A.; Arruda, M. A. Z.; Ferreira, S. C. L. Reproduced by permission of Taylor & Francis Group, LLC., <http://www.taylorandfrancis.com>.

viewed,²⁹ with a new literature application for determining manganese in samples of saline petroleum effluents by FAA spectroscopy, using 2-(2'-thiazolylazo)resorcinol (TAR) as the complexing agent.³⁰

2.1.1.6. Greening through Screening. Another way to reduce solvent is through screening. Although screening techniques are not uniquely green, screening reduces the number of samples run and therefore the amount of reagents and solvent used. A simple green prescreening technique was

used to identify dairy samples containing synthetic colorants. Using acetic acid solution as an eluent, a simple cotton/wool column retained the synthetic dyes.^{31,32} Positive samples were sent on to a liquid chromatograph for quantification.

2.1.2. Solvent Elimination

Liquid–solid extractions provide the opportunity to eliminate solvents in the pretreatment process because the analyte can be directly extracted from the liquid sample onto the solid sorbent material. These techniques, solid-phase extraction (SPE) and solid-phase microextraction (SPME, Figure 5), are well established.^{6,18,24} A SPME is easily coupled through thermal desorption to GC or gas chromatography–mass spectrometry (GC-MS), providing a truly green, solvent-free procedure.³³ A wide variety of sorbents are available commercially for the separation of organic and inorganic analytes, with more being developed, even using green synthetic principles.³⁴

Adaptations of the sorbants look to improve the extraction efficiencies of polar analytes and to allow their use in novel formats. Sorbant placements include stir bar sorption, to extract organochlorine compounds from SWE of soil samples followed by thermal desorption into GC-MS instruments,²² and hollow fiber sorbants used for liquid–liquid–liquid separations where the three liquids were an aqueous donor phase, organic solvent impregnated onto the solid-phase, and an aqueous acceptor phase filling the internal volume of the fiber. These have been applied to the extraction of phenoxy herbicides in bovine milk³⁵ and freely dissolved chlorophenols.³⁶

Although each individual chromatographic separation may use only a few milliliters of solvent, chromatographic separations can use an enormous amount of solvents annually. Adapting solid phases to allow water as the mobile phase is a significant step toward greening. A recent literature report described a modified silica with a thermoresponsive copolymer, poly(*N*-isopropylacrylamide-co-*n*-butylmethacrylate), to allow separation of phenylthiohydantoin (PTH) amino acids for *N*-terminus analysis of proteins by Edman degradation in an aqueous solvent.³⁷

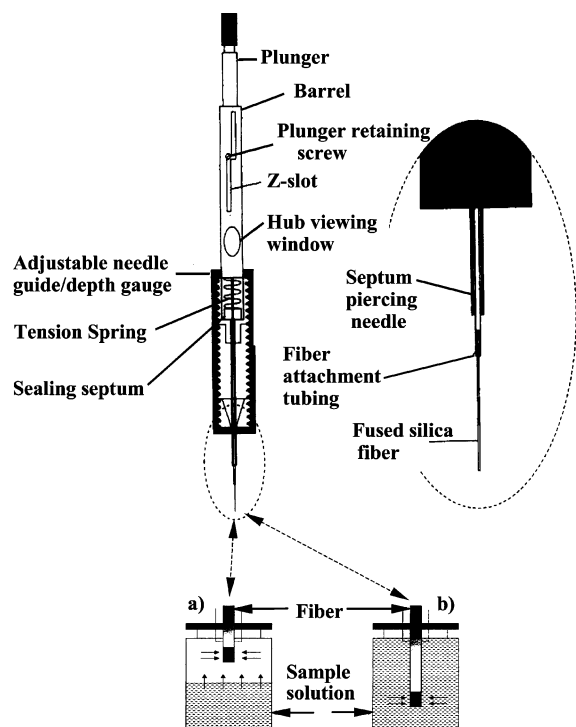


Figure 5. Solid-phase microextraction device with the sorbent material attached to the surface of the fiber and two modes of operation: (a) headspace and (b) direct liquid phase (immersion). Wrobel, K.; Kannamkumarath, S.; Wrobel, K.; Caruso, J. A. *Green Chemistry* **2003**, *5*, 250—Reproduced by permission of The Royal Society of Chemistry.

2.1.3. Derivatization of Molecules and Surfaces

The need to derivatize an analyte usually increases the environmental impact of an analysis, through the increased use of reagents and solvents, and reduces the quality of the results by adding possibilities for contamination or analyte loss. This includes derivatization of individual molecules as well as derivatization of a sorbent. A recent paper describes a green methanolysis procedure as part quantification of fatty acids in vegetable oils. Fatty acids are generally methylated to make fatty acid methyl esters (FAMEs) using a BF_3 -methanol procedure. In this report, an aliquot of the vegetable oil dissolved in dimethyl carbonate (DMC) was pyrolyzed with TiSiO_4 on-line with gas chromatography.³⁸ For green chemistry, the ideal situation is to eliminate the need for a derivatization, in accordance with Principle No. 8 in Table 1. However, if derivatization is still required for analysis, the use of less hazardous chemicals is a step toward a greener methodology, as in the example above.

2.2. Greening Signal Acquisition

There are limited opportunities to improve the greenness of analysis at the point of signal acquisition in established techniques because the act of acquiring a signal is generally quite green already. However, there have been opportunities to reduce hazardous chemical usage in at least three techniques in the recent literature: spectroscopy, electrochemistry, and bioanalytical chemistry.

2.2.1. Spectroscopy

In general, signal acquisition in spectroscopic techniques is rather green. Sample sizes are small, and there is little or no sample preparation or use of hazardous chemicals. A few

of the inherently green spectroscopic methods are atomic absorption, infrared, Raman, and XRF. A method of greening spectroscopy by extending the useful range is by using liquid core waveguides (LCWs). LCWs provide an opportunity to use long flow paths without the inherent attenuation of the incident light (Figure 6). The long path reduces the required

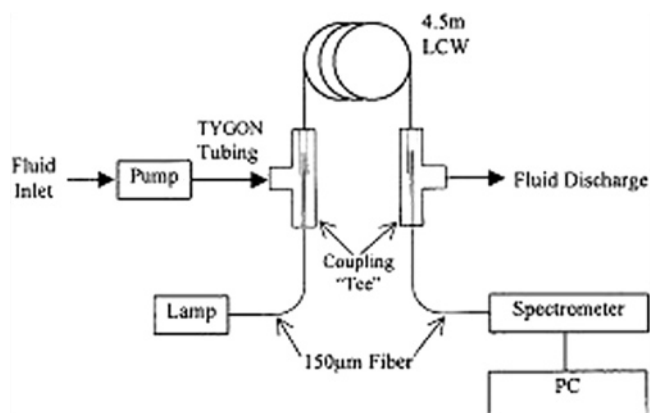


Figure 6. Long path length absorbance spectroscopy experimental setup. Reprinted with permission from Yao, W.; Byrne, R. H.; Waterbury, R. D. *Environmental Science and Technology* **1998**, *32*, 2646. Copyright 1998 American Chemical Society.

sample volume and, consequently, the solvent and reagents necessary to develop the chromophores. This has successfully been applied to nitrate/nitrite and phosphate analysis in natural waters.^{39,40}

2.2.2. Electrochemistry

Electrochemistry is a unique area of analytical chemistry where sample treatment has historically been relatively green but a hazard has come in the form of the mercury working electrode. Research has dramatically improved the greenness of electrochemistry by developing environmentally benign modified carbon as the basis for working electrodes, such as bismuth-coated carbon for anodic stripping voltammetry,⁴¹ and new ion selective electrodes.⁴² Carbon-based electrodes, particularly nanotubes and nanofibers,⁴³ have proven to be readily adaptable as electrochemical biosensors through the immobilization of biomolecules such as enzymes, antibodies, and whole cells.⁴⁴ Specific examples of electrochemical biosensors from the recent literature include glucose,⁴³ nitrate,⁴⁵ and polyphenol biosensors.⁴⁶

2.2.3. Bioanalytical Chemistry

Bioanalytical methods are often green due to the highly selective nature of the reactions, which usually removed the need for further separations or concentration steps, improving the greenness of the methods. As exemplified by the new electrochemical biosensors, bioanalytical chemistry is a rich area of development, providing original sensitive analyses as new biologically reactive chemical pairs are developed. Although classic enzymatic methods for the quantification of sugars by spectroscopy are still being adapted,⁴⁷ there are a number of novel bioanalytical techniques in the recent literature. These include an enzyme-linked immunosorbent assay (ELISA) for detection of [4-arginine]microcystins,⁴⁸ a fiber optic biosensor for atrazine using immobilized glutathione *S*-transferase I (GST-I) in a sandwich device with bromocresol green,⁴⁹ a luminescent protein, aequorin, developed for high throughput screening (HTS) as an alterna-

tive to radiolabeled assays,⁵⁰ as well as a photometric analysis of nitrate using corn leaf nitrate reductase.⁵¹

2.3. Greening with Automation and Flow Techniques

Automation of analytical chemistry reduces sample size, as well solvent and reagent consumption, significantly greening existing methods. The sophistication of the automation can vary from simple autosamplers with integrated analysis steps, such as hyphenated systems, to complex flow injection analysis (FIA), sequential flow injection analysis (SIA), and multicommutation flow systems, and on to fully contained microdevices.

2.3.1. Flow Injection Analysis (FIA) and Sequential Flow Injection Analysis (SIA)

First described over 30 years ago, FIA is a continuous flow method where the sample is injected into a carrier stream, usually containing reagents. As the sample disperses, it reacts with reagents. Mixing continues during downstream flow until the mixture reaches a detector, typically an electrochemical or spectrophotometric device. The physical mixing of the chemicals and the extent of reactions between the chemicals are incomplete, typically giving a throughput advantage. Precisely timed injection events and controlled flow rates in the manifold reduce noise to allow high reproducibility of these transient signals.⁵² Typical flow rates are 1–2 mL/min, with the sample size in the range of 10–100 μL with a throughput of 1–2 samples/min. Recent literature references extend the use of FIA by adding solid-phase reagents to analyze for nitrate in surface water by adding an anion-exchange resin for in-line separation of interfering species,⁵³ to analyze for chlorpyrifos, a pesticide, using chemiluminescence by immobilization of the periodate and luminol on an anion-exchange column (Figure 7),⁵⁴ and

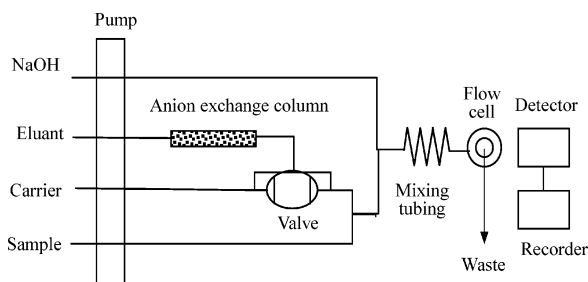


Figure 7. Schematic diagram of the flow injection system. Reprinted with permission from Song, Z.; Hou, S.; Zhang, N. *Journal of Agricultural and Food Chemistry* **2002**, *50*, 4468. Copyright 2002 American Chemical Society.

to analyze for chloride by using a fixed-bed of immobilized $\text{Hg}(\text{SCN})_2$.⁵⁵ The use of FIA in this procedure led to a 400% reduction in Hg waste compared to conventional spectroscopy for the same method. Simple FIA has been adapted for postanalysis in-line waste detoxification, such as the TiO_2 catalyzed UV mineralization of aromatics,⁵⁶ with the more recent development of cyclic FIA where recycling the reagent solutions further reduces the use of toxins, as is the case with the determination of lead with Arsenazo III.⁵⁷ Herein, Arsenazo III was regenerated on-line using a cation-minicolumn which also collected the heavy metal analyte.

A more recent adaptation of FIA is SIA, in which zones of sample and reagent are sequentially injected, forming a linear stack. Reversible flow paths and flow acceleration are

used to promote mixing before moving the sample/reagent mixture to the detector. These adaptations reduce the use of reagents and carrier in SIA to about a tenth of that used with FIA. Recent literature includes extensions of this technology into turbidity to quantify phosphate in urine by the crystallization of calcium phosphate or by the inhibition of the precipitation of calcium carbonate⁵⁸ and into linking SIA with on-line ultrasonic extraction of mercury from water and urine.⁵⁹

2.3.2. Multicommutation

Multicommutation is an adaptation of flow injection that utilizes multiple solenoid valves as separate switching devices to create a more flexible flow path that is able to use significantly less reagents than FIA. Recent literature includes an automated procedure to quantify cyclamate by reaction of nitrite and subsequent spectrophotometric determination of excess nitrite by iodometry,⁶⁰ utilizing less than 3 mg of KI and 2.0 mL of effluent per sample, as well as phenol in water by oxidative coupling to 4-aminoantipyrine in the presence of hexacyanoferrate(III).⁶¹ This method utilized a long path length optical cell that, together with the multicommutation analysis, increased the method sensitivity enough to obviate the need for preconcentration in chloroform. Another example is application of multicommutation to vibrational spectroscopy by the infrared determination of benzene in gasoline.⁶²

2.4. Green by *in-Situ*

The ideal green analysis would run *in-situ* without sampling or adding reagents and could achieve all of the green chemistry principles related to analytical methods. An important new concept that the U.S. EPA is promoting is the “Triad Approach”. It is an innovative approach to decision-making that proactively exploits new characterization and treatment tools.⁶³ The triad refers to three primary components: systematic planning, dynamic work strategies, and real-time measurement systems. The most important of these three components for green analytical chemistry is real-time measurement techniques that typically do not use chemicals for preservatives or extractions or that use small amounts of them. A triad approach that includes real-time measurements effectively implements green analytical chemistry as well as serves to provide a less expensive analytical methodology.

Some traditional methods approaching *in-situ* work, including XRF and ATR-IR, have already been mentioned above. New techniques are under development, with a variety of names, including lab-on-a-chip technology, on-line analysis, real-time monitoring, and field sensors. Moving technologies from the analytical bench into reactors or the field requires clever application of techniques previously mentioned herein. Sorbants (SPE and SPME) are a method to extract samples *in-situ* and store samples for analysis at a secondary location. New field samplers have been developed for SPME,⁶⁴ and a rolling stir bar sampling procedure has been developed for sampling volatile organic compounds from agricultural products, plant materials, and human skin for thermal desorption/GC-MS.⁶⁵ Microfluidic devices and lab-on-a-chip technology are still largely under development and primarily in the bioanalytical regime⁶⁶ with recent literature examples including capillary electrophoresis microchips,⁶⁷ microfluidic SPE for sample preconcentration,⁶⁸ and membrane-implanted analysis for cholesterol.⁶⁹ While

in the field, metals in marine environments can be detected *in-situ* by a portable spectrophotometric analysis system that uses LCW, demonstrated in an estuary in Tampa Bay, FL,⁷⁰ or by electrochemical stripping, demonstrated in San Diego Bay, CA.⁷¹

3. NEMI and Greener Analytical Methods

Although it is difficult to identify trends in green analytical chemistry in the literature, until now it has been impossible to quantitatively compare the greenness of analytical methods due to a lack of discriminatory criteria. The ACS Green Chemistry Institute has developed “greenness” criteria for environmental methods as a way to identify analytical chemistry methods that use fewer harmful solvents, use safer chemicals, and minimize waste. These criteria have been applied to the National Environmental Methods Index (NEMI). NEMI is a free Internet-searchable database of environmental methods located at www.nemi.gov (Figure 8).⁷² The database currently contains information (method

Figure 8. NEMI homepage at www.nemi.gov.⁷²

summaries, metadata, and links to many full methods) for over 800 methods. With the addition of greenness profiles, and the data behind them, to the vast information in NEMI, users can make a more informed method selection (now through the Analyte Search BETA page). However, the primary consideration must always be that any method selected should meet the performance characteristics (e.g., detection level, acceptable bias and precision, etc.) needed by the user, irrespective of how “green” it is.

3.1. Background of NEMI

NEMI is one of the tools developed by the Methods and Data Comparability Board (MDCB). The MDCB is a partnership of water-quality and environmental monitoring experts.⁷³ The ACS Green Chemistry Institute has worked closely with the MDCB to provide greenness profiles of analytical methods in NEMI.

This database, which was publicly released in 2002, continues to be expanded to include a growing number of methods and types of methods. Although NEMI is the largest database of environmental analytical methods, it still contains only a fraction of those available. The vast majority of the 800+ methods in NEMI are for use with the water medium. However, the database was constructed to include methods designed for other media (e.g., air, animal tissue, soils/sediment, various, and other), and there are a few methods representative of these media.

Initial methods were submitted by the U.S. Environmental Protection Agency (EPA) and the U.S. Geological Survey (USGS). Now, methods are also sought and provided by scientific organizations (e.g., ASTM and Standard Methods) as well as by private companies. There is no charge to enter methods into NEMI. To be eligible for inclusion, a method must be written in a procedural format and published (i.e., be publicly accessible so that others may obtain it and use it). Through NEMI, the user can access method summaries as well as the full method document. Within the database, methods can be easily searched, sorted, and compared. The current search field options include analyte (name or CAS number), media type (water, air, soil/sediment, or tissue), instrument and detector (over 80 choices), method subcategory (biochemical, organic, inorganic, microbiological, physical, or radiochemical), and method source (USGS, EPA, ASTM, Standard Methods, and many others). In addition, performance characteristics of methods can be easily compared in a search results table, including detection level and limit type, bias, precision, spiking level, and cost.⁷⁴

3.2. Greenness Profiles of Greener Analytical Methods

In order to provide greenness profiles, acceptance criteria were developed and applied to the methods. Acceptance criteria translate the data from an analytical method (including chemicals used, pH, and waste generated) into a greenness profile. The profile criteria are summarized by four key terms: PBT (persistent, bioaccumulative, and toxic), Hazardous, Corrosive, and Waste. These profile criteria were carefully defined and developed in collaboration with over 25 environmental methods experts from more than 5 U.S. Federal agencies and private labs in December 2005. It was the consensus of the experts that these were the most important criteria both from a regulatory view as well as from those that directly relate to the 12 Principles of Green Chemistry referenced earlier. On the regulatory side, the EPA’s Toxic Release Inventory (TRI) chemicals list,⁷⁵ the PBT chemicals identified on the TRI list,⁷⁵ and the Resource Conservation and Recovery Act (RCRA)’s D, F, P, and U hazardous waste lists and characteristics of hazardous wastes, such as the definition of corrosive,⁷⁶ were referred to when developing the acceptance criteria definitions. Although an energy criterion was also desired as part of a greenness profile, a way to consistently evaluate energy use in a method could not be readily devised, so energy was not included. The profile criteria that make a method “less green” are defined as follows.

A method is “less green” if

1. PBT—a chemical used in the method is listed as a PBT, as defined by the EPA’s TRI⁷⁵
2. Hazardous—a chemical used in the method is listed on the TRI⁷⁵ or on one of the RCRA’s D, F, P or U hazardous waste lists⁷⁶

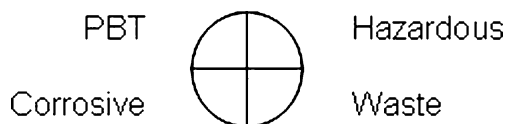


Figure 9. The greenness profile symbol.

3. Corrosive—the pH during the analysis is <2 or >12
4. Waste—the amount of waste generated is >50 g.

A greenness profile symbol (Figure 9) was developed to provide an easily recognized summary of the greenness profile of the method. This four-quadrant circle with the quadrants labeled as PBT, Hazardous, Corrosive, and Waste represents the acceptance criteria. If a method is identified as NOT being “less green” as defined in the above profile criteria, the quadrant(s) associated with that acceptance criterion is filled-in (with green color). If a method is identified as being “less green” as defined in the above profile criteria, the quadrant(s) associated with that acceptance criterion is left blank (not filled-in). The result is the greenness profile symbol. For example, if a method does not contain any chemicals on the TRI or RCRA lists, the Hazardous quadrant would be filled-in green. When an analyte search is conducted in NEMI, the greenness profile symbols appear in a column of the search result table.

The greenness of a method is relative, and the bar between “less green” and greener has been set by the acceptance criteria defined above.

3.3. Application of Greenness Profiles

Specific data, including the sample size that is worked-up for analysis, chemicals used and amounts (to which the PBT and Hazardous acceptance criteria #1 and #2 are applied), pH (to which the Corrosive acceptance criterion #3 is applied), and waste amount generated (to which the Waste acceptance criterion #4 is applied), were collected from the full analytical methods currently in NEMI in order to generate a greenness profile for each method. When analyte searches are conducted in NEMI, the search result table contains a column for the greenness profile symbols. From this column, the user can easily compare the greenness profiles of the methods in addition to the other method performance criteria and information in the other search result table columns. Furthermore, the user can access the detailed data from the method that was used to generate the greenness profile by selecting the symbol.

For example, if a method is desired that will have regulatory acceptance to measure the pesticide aldrin in water, a search of NEMI would return two methods from EPA’s National Exposure Research Laboratory (EPA-NERL), Methods 525.2⁷⁷ and 505,⁷⁸ that meet the performance criteria of a detection level of 0.2 $\mu\text{g/L}$ or lower and a precision with a relative standard deviation (RSD) of no greater than 20% (Figure 10).⁷² From the greenness profile symbols of the two methods, Method 525.2 has the PBT quadrant filled-in green while Method 505 has the Corrosive, PBT, and Waste quadrants filled-in green, as illustrated in parts a and b, respectively, of Figure 11.

Clearly, Method 525.2 is the “less green” method of the two by this greenness profile definition and comparison. This is because Method 525.2 uses ethyl acetate (on RCRA F and U lists), methylene chloride (on TRI and RCRA F and U lists), and methanol (on TRI and RCRA F and U lists) to extract a 1 L sample. In addition, the pH is less than 2, and

more than 50 g of waste is generated. As a result, the greenness profile symbol has only the PBT quadrant filled-in green, since no PBTs are used in the method. In contrast, Method 505 extracts 35 g of sample with only 2 mL of hexane (on the TRI list). The pH of the sample is not made acidic or basic, and less than 50 g of waste is generated. As a result, three out of four quadrants of the greenness profile symbol are filled-in green. In this example, if Method 505 meets all analytical requirements, then this method may be selected over Method 525.2 because of a better greenness profile.

3.4. Characteristics of Greener Analytical Methods in NEMI

Over two-thirds of the methods in NEMI had sufficient information so that they could be evaluated for greenness using the greenness profiles described above. The most common reasons for inability to evaluate greenness profiles for methods are summarized as follows:

(1) The most frequent reason why a method could not be evaluated was lack of information on sample size and/or chemicals used (e.g., U.S. Geological Survey (USGS) method number I-5270,⁷⁹ American Society for Testing and Materials (ASTM) method number D6502,⁸⁰ and EPA-NERL method number 206.5⁸¹).

(2) In other cases, the full method was not available electronically or was a generally inaccessible book, manual, or CD (e.g., U.S. Department of Energy Environmental Measurements Laboratory (DOE_EML) method number G-03,⁸² EPA Engineering and Analysis Division (EPA-EAD) method number 1636,⁸³ USGS method number O-3113,⁸⁴ and EPA-NERL method number 231.1⁸⁵).

(3) Occasionally, parts of the procedure used for analysis are not printed in the method and instead are referenced as being in another source (e.g., ASTM method D5613⁸⁶ and EPA Office of Solid Waste (EPA-OSW) 8000 series methods⁸⁷).

However, among the 560 methods that were able to be evaluated using the greenness profiles, some characteristic trends were noted among those methods. The comparisons below are organized according to the four greenness profile criteria. This organization is highlighting a particular criterion, and while some of the methods would be identified as “less green” by multiple criteria, only a single criterion is emphasized in each grouping below.

The most frequent cause of a method to be “less green” was a failure to meet the requirements of the Waste greenness criterion; that is, the method generated greater than 50 g of waste. Two-thirds of the evaluated methods failed the waste greenness criterion. Of these methods, the ones testing for organic compounds frequently used large sample sizes and used relatively large amounts of solvents for extraction. Examples include the following:

(1) EPA-NERL method number 625,⁸⁸ which uses 430 mL of methylene chloride to extract semivolatiles from a 1 L water sample for GC-MS analysis,

(2) USGS National Water Quality Laboratory (USGS-NWQL) method number O-1104,⁸⁹ which uses 75 mL of hexane to extract organochlorine and organophosphorus compounds from a 1 L water sample for GC with flame photometric detection or electron capture detection (ECD), and

(3) ASTM method number D5475,⁹⁰ which uses 22 mL of methyl *tert*-butyl ether and 441 mL of methylene chloride

National Environmental Methods Index

Analyte (main) Search General Search Regulatory Search Multi-Analyte Search Analyte Search BETA

This is the beta version of an Analyte Query that includes a "Greenness" Rating by the Green Chemistry Institute.

This page is currently under construction, so features may be added or removed before it goes to production. Feel free to test and submit **comments** on its functionality. If something appears "broken", wait several hours or a day and try again--there is active development going on on this page.

Select Search Criteria

Analyte Name or Code (required)

Analyte Name:

- OR -

Analyte Code:

Media Name*:

Method Source*:

Instrumentation*:

Method Subcategory*:

* optional

View Results in a New Window (Printable Format)
Export results for Microsoft Excel
Export results as a tab separated text file (can be opened in any text editor or spreadsheet)

Analyte: Aldrin (309-00-2) [Click for list of synonyms](#)

6 methods were found in NEMI that match your criteria for the analyte aldrin.

Criteria Summary:

- Media Name equals WATER ORA-01403: no data found

Method Number (Sort)	Source (Sort)	Method Descriptive Name (Sort)	Detection Level	Detection Level Type	Bias	Precision	Spiking Level	Instrumentation	Relative Greenness Cost (Sort)	Profile
505	EPA-NERL	Pesticides and PCBs in Water GC-ECD	.007 ug/L	MDL	106 % Rec. (SL)	20 RSD. (SL)	.05 ug/L	GC-ECD	\$\$\$	⊕
508	EPA-TSC/NERL	Chlorinated Pesticides in Water Using GCECD	.014 ug/L	MDL	66 % Rec. (SL)	9 RSD. (SL)	.075 ug/L	GC-ECD	\$\$\$	⊕
508.1	EPA-OGWDW/TSC	Chlorinated Pesticides, Herbicides, and Organohalides in Water by GCECD	.009 ug/L	MDL	80 % Rec. (SL)	37.5 RSD. (SL)	.01 ug/L	GC-ECD	\$\$\$	⊕
525.2	EPA-NERL	Organics in Water Using GCMS	.11 ug/L	MDL	80 % Rec. (SL)	9.3 RSD. (SL)	.5 ug/L	GC-MS	\$\$\$	⊕
608	EPA-EAD	Organochlorine Pesticides and PCBs via GC with Electron Capture Detector (ECD)	.004 ug/L	MIDL	85 % Rec. (ML)	19 RSD. (ML)	1 ug/L	GC-ECD	\$\$\$	⊕
625	EPA-NERL	Base/Neutral and Acid Organics in Wastewater	1.9 ug/L	MDL	95 % Rec. (ML)	55 RSD. (ML)	10 ug/L	GC-MS	\$\$\$	⊕

www.nemi.gov
Maintained by djsullivan@usqs.gov

Figure 10. The search results in the Analyte Search Beta screen of NEMI, for a search of the analyte aldrin in water in the organic methods from the U.S. EPA. Six results match the search criteria, with EPA-NERL method numbers 525.2 and 505 included. The greenness profiles are in the far right column.⁷²

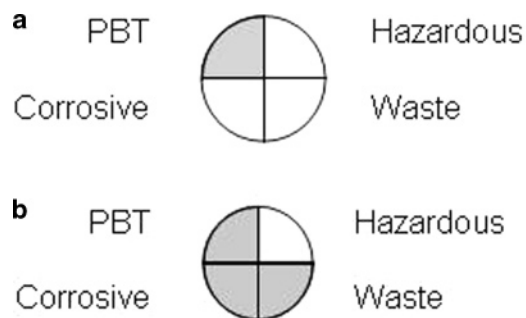


Figure 11. Greenness symbols for two methods measuring pesticide in water by gas chromatography: EPA-NERL method numbers (a) 525.2 and (b) 505.

to extract nitrogen and phosphorus pesticides from a 1 L water sample for analysis by GC with a nitrogen–phosphorus detector.

In contrast, examples of organic methods that pass the greenness waste criterion, generating less than 50 g of waste, include the following:

(1) Standard Methods number 6610B,⁹¹ which injects a 1 mL aliquot of a 25 mL water sample for HPLC separation of carbamate pesticides followed by direct-injection post-column derivatization and detection by fluorescence,

(2) EPA-NERL method number 502.2,⁹² which uses 5 mL of water sample purged with an inert gas to strip volatile organic chemicals that are then trapped (Figure 12) and analyzed by GC with a photoionization detector and electrolytic conductivity detector in series, and

(3) Strategic Diagnostics method number 73310,⁹³ which uses less than 0.1 mL of water sample and the ELISA immunoassay technique mentioned in section 2.2.3.

Inorganic methods also frequently fail the waste greenness criterion because strong mineral acids are added to samples for preservation or digestion. If the waste quantity, which

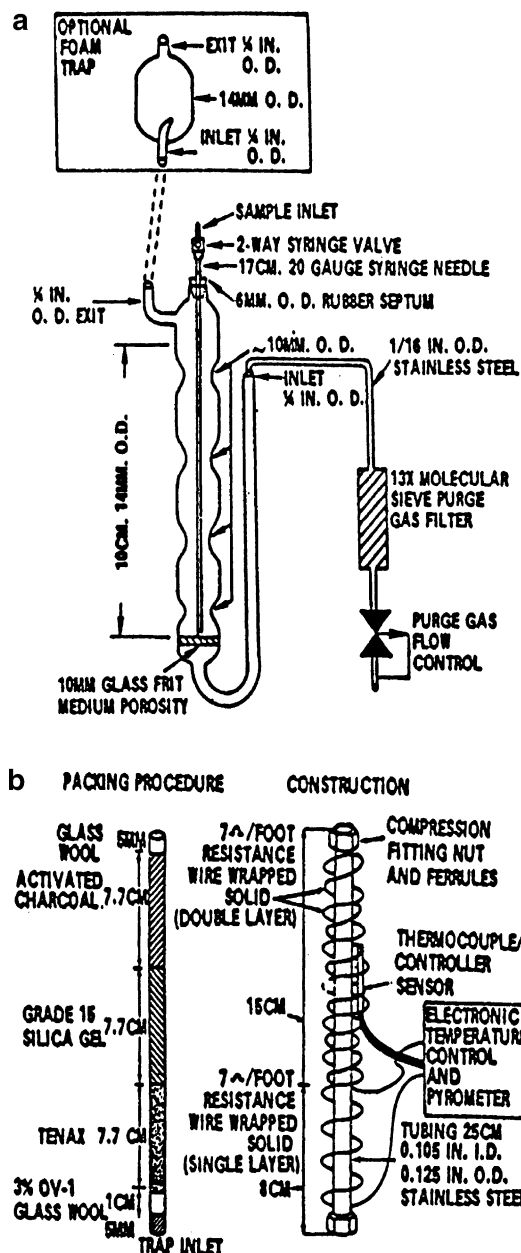


Figure 12. Diagrams of (a) purging device and (b) trap packings and construction to include desorb capability.⁹²

includes any chemically treated sample, exceeds 50 g, it fails the waste greenness profile criterion. Examples include the following:

(1) Standard Methods number 3120B,⁹⁴ where 8 mL of nitric acid and 10 mL of 50% hydrochloric acid are added to 100 mL of a water sample in preparation for measuring metals by inductively coupled plasma (ICP) with atomic emission spectroscopy,

(2) DOE method number MM800,⁹⁵ where 118 mL of various concentrations of nitric and hydrochloric acids are added to 100 mL of a water sample for measurement of uranium by ICP-MS, and

(3) USGS-NWQL method number I-3840,⁹⁶ where 10 mL of hydrochloric acid, 10 mL of iodine solution, and 12 mL of sodium thiosulfate solution are added to 100 mL of a water sample to measure sulfide by iodometric titration.

In contrast, inorganic methods that pass the greenness waste criterion include the following:

(1) EPA-NERL method number 200.8,⁹⁷ which uses only 20 mL of acidified water for sample preparation for analyzing metals by ICP-MS, even though 1 L of water is collected,

(2) EPA Office of Ground Water and Drinking Water Technical Support Center (EPA-OGWDW/TSC) method number 326.0,⁹⁸ which uses 0.25 mL of a 10 mL water sample separated by HPLC with a postcolumn reagent for trace bromate analysis by ion chromatography (IC).

(3) USGS-NWQL method number I-3239,⁹⁹ which uses a 10 mL water sample to which 1 mL of a 20% ammonium chloride solution is added followed by direct insertion into a FAA spectrometer for cobalt analysis.

The second most frequently found reason for a method to be “less green” was the use of hazardous chemicals (as defined in the greenness criterion #2 above) in the procedure. About half of the evaluated methods failed the hazardous greenness criterion. Examples include the following:

(1) EPA-NERL method number 410.1¹⁰⁰ for chemical oxygen demand (COD), which treats 50 mL of a water sample with 25 g of potassium dichromate solution, 1 g of mercuric sulfate solution, and 70 mL of sulfuric acid—silver sulfate solution prior to titration with ferrous ammonium sulfate,

(2) USGS-NWQL method number I-1232¹⁰¹ for Cr—VI analysis by FAA, which chelates the chromium in a 100 mL water sample with 5 g of ammonium pyrrolidine dithiocarbamate before extraction with 10 mL of methyl isobutyl ketone, and

(3) EPA-EAD method number 605¹⁰² for benzidines, which uses a separatory funnel extraction process involving a 1 L sample of water, 270 mL of chloroform, 24 mL of methanol, 30 mL of sodium hydroxide solution, 5 mL of sodium tribaric phosphate solution, and 75 mL of sulfuric acid solution prior to HPLC with an electrochemical detector.

In contrast, examples of the many methods that pass the hazardous greenness criterion include the following:

(1) USGS-NWQL method number I-3152¹⁰³ for total calcium in water, which uses a 10 mL water sample with 1 mL of lanthanum chloride solution that is analyzed by direct insertion into a flame AA spectrometer,

(2) IDEXX method SimPlate¹⁰⁴ for heterotrophic bacteria in water, which uses a 10 mL water sample and incubation of the bacteria (Figure 13), and



Figure 13. SimPlate for the quantification of heterotrophic plate counts in water. Reprinted with permission from IDEXX, SimPlate for HPC Unit Dose.

(3) EPA-NERL method number 524.2¹⁰⁵ for volatile organic compounds in water, in which 40 mL of water is purged with an inert gas to trap the analytes on a solid sorbent material (using the same apparatus as in Figure 12) for GC-MS analysis.

Only 5% of the NEMI methods failed the PBT greenness criterion (as defined by criterion #1 above), and 100% of those also failed the hazardous chemical greenness criterion. The most commonly encountered PBTs in analytical methods are lead and mercury compounds. Examples of methods being less green because of chemicals on the PBT list being used include the following:

(1) EPA-NERL method number 335.2¹⁰⁶ for cyanide analysis by a titrimetric or colorimetric procedure (depending on cyanide concentration), in which sulfide is removed from the water sample with a scrubber containing 25 mL of 3% lead acetate solution,

(2) ASTM method number D1252B¹⁰⁷ for COD determined spectroscopically, in which 1.5 mL of a digestion solution that contains mercuric sulfate is added to a 2.5 mL sample of water in a microscale analysis, and

(3) Standard Methods method number 3500-VB,¹⁰⁸ where vanadium is measured spectroscopically after 1 mL each of ammonium persulfate–phosphoric acid, gallic acid, and mercuric nitrate solutions are added to 10 mL of a water sample.

In those last two examples, while the method is still considered “less green” because of the use a PBT, the quantities of mercury are extremely small in the microscale analyses. However, a greener approach would be to use a method that does not require any mercury.

The last of the greenness profiles to be evaluated is criterion #3 for corrosive samples. About one-fifth (i.e., 101) of the evaluated methods were “less green” because the pH of samples was adjusted to either <2 or >12. Examples of these methods include the following:

(1) EPA-NERL method number 200.8⁹⁷ for metals in water analysis by ICP-MS, where the pH of the 20 mL sample prepared for analysis is reduced by nitric acid to <2,

(2) EPA-EAD method number 604¹⁰⁹ for phenols in water by GC-ECD or flame ionization detection, where the pH of a 1 L sample of water is raised to >12 by sodium hydroxide solution prior to extraction with methylene chloride and then lowered to <2 by sulfuric acid solution for a second extraction, and

(3) Standard Methods number 6251B¹¹⁰ for haloacetic acids and trichlorophenol by GC-ECD, in which the pH of a 30 mL water sample is adjusted to <0.5 using 98% sulfuric acid, the sample is extracted with methyl *tert*-butyl ether, and then the extracted compounds are methylated with diazomethane solution prior to analysis.

4. Conclusion

Green chemistry is a vibrant area of research within analytical chemistry, as this review clearly demonstrates. Undoubtedly, there already exist many green techniques in the literature and methods in the NEMI database, but they have rarely been collected in a manner that highlights these environmentally benign procedures or is useful to the individual analyst. The primary goal of all analytical chemists is to provide accurate and precise information. While the greenest methods cannot be used in every situation, the literature described herein and the greenness profiles and acceptance criteria in the NEMI database can provide

guidance on how to identify and further develop “greener” methods benefiting the profession and the environment.

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