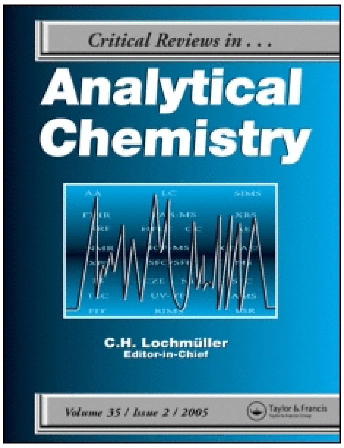

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Green Chemistry and the Role of Analytical Methodology Development

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ABSTRACT: Green Chemistry has emerged in the 1990s as a way that the skills, knowledge, and talents of chemists can be used avoid threats to human health and the environment in all types of chemical processes. One of the most active areas of Green Chemistry research and development is in analytical methodology development. New methods and techniques that reduce and eliminate the use and generation of hazardous substances through all aspects of the chemical analysis lifecycle are the manifestations of the recent interest in Green Analytical Chemistry.

I. INTRODUCTION

Green Chemistry is an approach to the synthesis, processing, and use of chemicals that reduce risks to humans and the environment. Many innovative chemistries have been developed over the last several years that are effective, efficient, and more environmentally benign. These approaches include new syntheses and processes as well as new tools for instructing aspiring chemists how to do chemistry in a more environmentally benign manner. The benefits to industry as well as the environment are all a part of the positive impact that Green Chemistry is having in the chemistry community and in society in general.

Over the last few years, the chemistry community has been mobilized to develop new chemistries that are less hazardous to human health and the environment. This new approach has received extensive attention[1-16] and goes by many names, including Green Chemistry,[17-19] Environmentally Benign Chemistry, Clean Chemistry, Atom Economy[20] and Benign By Design Chemistry.[21] Under all of these different designations there is a movement toward pursuing chemistry with the knowledge that the consequences of chemistry do not stop with the properties of the target molecule or the efficacy of a particular reagent. The impacts of the chemistry designed by chemists are felt by the people that come in contact with the substances that they make and use and by the environment in which they are contained.

For those who have been given the capacity to understand chemistry and practice it as a livelihood, it is and should be expected that this capacity will be used wisely. With knowledge comes the burden of responsibility. Chemists do not have the luxury of ignorance and cannot turn a blind eye to the effects of the science that is created. Because there is the ability to develop new chemistries that are more benign, chemists are obligated to do so.

Chemists from all over the world are using their creativity and innovation to develop new synthetic methods, reaction conditions, analytical tools, catalysts, and processes under the new paradigm of Green Chemistry. It is a challenge for the chemistry community to look at the excellent work that has been and continues to be done and to ask the question, “Is the chemistry I am doing the most benign that I can make it?”.

One obvious but important point: nothing is benign. All substances and all activity have some impact just by their being. What is being discussed when the term benign by design or environmentally benign chemistry is used is simply an ideal. Striving to make chemistry more benign wherever possible is merely a goal. Much like the goal of “zero defects” that was espoused by the manufacturing sector, benign chemistry is merely a statement of aiming for perfection.

Chemists working toward this goal have made dramatic advances in technologies that not only address issues of environmental and health impacts but do so in a manner that satisfies the efficacy, efficiency, and economic criteria that are crucial to having these technologies incorporated into widespread use. It is exactly because many of these new approaches are economically beneficial that they become market catalyzed. While most approaches to environmental protection historically have been economically costly, the Green Chemistry approach is a way of alleviating industry and society of those costs.

II. THE ELEMENTS OF GREEN CHEMISTRY

While it has already been mentioned that nothing is truly environmentally benign, there are substances that are known to be more toxic to humans and more harmful to the environment than others. By using the extensive data available on human health effects and ecological impacts for a wide variety of individual chemicals and chemical classes, chemists can make informed choices as to which chemicals would be more favorable to use in a particular synthesis or process. 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.

Green Chemistry is a fundamental and important tool in accomplishing pollution prevention. Pollution prevention is an approach to addressing environmental issues that involves preventing waste from being formed so that it does not have to be dealt with later by treatment or disposal. The Pollution Prevention Act of 1990[22] established this approach as the national policy of the U.S. and the nation's "central ethic"[23] in dealing with environmental problems.

There is no doubt that over the last 20 years, the chemistry community, and in particular the chemical industry, has made extensive efforts to reduce the risk associated with the manufacture and use of various chemicals. There have been innovative chemistries developed to treat chemical wastes and remediate hazardous waste sites. New monitoring and analytical tools have been developed for detecting contamination in air, water, and soils. New handling procedures and containment technologies have been developed to minimize exposure. While these areas are laudable efforts in the reduction of risk, they are not pollution prevention or Green Chemistry, but rather are approaches to pollutant control. Many different ways to accomplish pollution prevention have been demonstrated and include engineering solutions, inventory control, and "housekeeping" changes. Approaches such as these are necessary and have been successful in preventing pollution, but they also are not Green Chemistry. There is excellent chemistry that is not pollution prevention and there are pollution prevention technologies that are not chemistry. Green Chemistry is using chemistry for pollution prevention.

No one who understands chemistry, risk assessment, and pollution prevention would claim that assessing which substances or processes are more environmentally benign is an easy task. To the contrary, the implications of changing from one substance to another are often felt throughout the lifecycle of the product or process. This difficulty for obtaining a quantifiable measurement of environmental impact has been, however, too often used historically as a rationale for doing nothing. The fact is that for many products and for many processes, clear determinations can be made. Many synthetic transformations have clear advantages over others, and certain target molecules are able to achieve the same level of efficacy of function while being significantly less toxic.

It is important that chemists develop new Green Chemistry options even on an incremental basis. While all elements of the lifecycle of a new chemical or process may not be environmentally benign, it is nonetheless important to improve those stages where improvements can be made. The next phase of an investigation can then focus on the elements of the lifecycle that are still in need of improvement. Even though a new Green Chemistry methodology does not solve at once every problem associated with the lifecycle of a particular chemical or process, the advances that it does make are nonetheless very important.

There are many advances currently being made in Green Chemistry that are everything from incremental to universal in their impact on the problems that they are addressing. The work in this field is pioneering and highly innovative and will provide an information data set of proven Green Chemistry methods and techniques that chemists in the future will need in order to be able to design entire synthetic pathways and processes that are more environmentally benign.

Green Chemistry is carrying out chemical activities, including chemical design, manufacture, analysis, use, and disposal, such that hazardous substances will not be used and generated. This is a very simple yet global view of how the field of chemistry should be perceived and practiced. Intrinsic to this definition is the recognition that chemists, as architects of matter, have in their power the ability to design products and processes that possess the properties they desire. Green Chemistry simply states that a central property or performance criterion of any chemical activity must be that it is benign to human health and the environment.

Of course, no chemical activity is ever completely innocuous or totally benign to human health and the environment. Just as many companies have adopted goals of ‘zero accidents’ or ‘zero defects’, it is recognized that any goal of perfection is not fully attainable. It is also recognized that in setting such a goal, the value lies not in the actual goal but in the process of striving toward that goal. Striving toward nothing less that perfection ensures that improvements will always be sought in each step of the process.

The goal of Green Chemistry is to reduce the hazards associated with products and processes that are essential not only to maintain the quality of life achieved by society through chemistry, but also to further advance the technological achievements of chemistry, and to do so in a sustainable manner. Throughout the evolution of the environmental movement, environmental policies, laws, and regulations have focused on quantifying the risk posed by chemicals in the environment. Risk can be summarized in simple terms as the product of the hazard of a particular substance and the exposure to that substance:

$$\text{Risk} = \text{Hazard} \times \text{Exposure}$$

Historically, approaches to minimizing the risk associated with chemical activity, as dictated by environmental laws and regulations, have almost universally involved minimizing the exposure to a chemical substance. This has been accomplished, for example, by controlling the concentrations of a chemical in an aqueous waste stream before release to a particular water body, using scrubbers on the end of smoke stacks to reduce emissions to air, or requiring the use of personal protective equipment such as respirators and gloves. These and a host of other environmental technologies have been designed, developed, and implemented to control or prevent exposure of hazardous chemicals to humans and the environment.

Green Chemistry seeks to reduce or eliminate the risk associated with chemical activity by reducing or eliminating the hazard side of the risk equation, thereby obviating the need for exposure controls and, more importantly, preventing environmental incidents from ever occurring through accident. If a substance poses no significant hazard, then it cannot pose a significant risk, and there is no need to limit the exposure to the substance. It should be noted that hazard is not simply defined as toxicity but rather includes the full range of consequences that can be realized from the use or generation of a substance. Hazard therefore includes, in addition to acute and chronic toxicity, carcinogenicity, and mutagenicity, properties such as explosivity, flammability, and corrosivity, direct ecological impacts such as plant and animal toxicity and atmospheric damage, and indirect ecological impacts such as resource depletion, global climate change, and persistence in the environment.

The enormous economic burden, discussed above, that has been associated with the ‘command and control’ approach to environmental protection during the last generation is due, in very large part, to the choice to reduce risk by controlling the exposure to a hazardous chemical substance rather than by reducing the hazard. This approach requires capital investments, technology development and implementation, human resources, and continuous vigilance to ensure that exposure will be and remain minimized. In contrast, choosing an innocuous substance rather than a hazardous substance should not be any more costly, but rather should provide cost incentives because of the obviated need for exposure controls.

Green Chemistry and the design and development of green chemical products and processes, as described in the articles that follow in this journal, follow the same tradition of scientific discovery and understanding that has characterized chemistry from its origins. Green Chemistry utilizes the information that is now available to the scientific community about the toxicity and other hazards posed by certain chemicals in order to fully evaluate the negative as well as positive impact of the chemistry being designed. Databases of information on the hazardous properties of chemicals have been available only recently. In previous years, the absence of this data meant that chemists could not effectively evaluate the consequences of the chemicals substances that were being designed and synthesized. Because this is no longer the case and the data exist, it is the responsibility of chemists and the chemical community to use this information.

Just as chemists need to fully understand the nature and source of environmental problems that result from certain chemicals of concern released to the environment, chemists are also required to use that understanding in preventing the problems from occurring in the first place. For a wide array of chemicals, the activity of a chemical of concern in the environment can be related to the molecular structure of the chemical, that is, how the atoms of the molecule are connected in. With a combination of a knowledge of the nature of a chemical’s hazardous properties with the ability to manipulate the chemical’s structure, a chemist possesses the ability and skill to mitigate the hazard.

The evaluation and elucidation of the various environmental problems that have occurred in the last several decades relied primarily on the work of analytical, physical, computational, and theoretical chemists conducting studies on atmospheric, aquatic, and terrestrial systems. Green Chemistry not only requires the talents of these subdisciplines of chemistry but also requires the subdisciplines of synthesis, organic and inorganic, catalysis, biochemistry, and materials science. Therefore, green Chemistry is applicable to all areas of chemistry. Green Chemistry is also applicable to all sectors of the chemical industry ranging from pharmaceuticals and specialty chemicals to the high volume manufacture of bulk chemicals. Green Chemistry technologies have been researched and developed in industry for both their environmental benefits as well as economic benefits and have been implemented successfully by some of the largest chemical producing companies in the world as well as by small businesses.

Advances have been made by both academia and industry in Green Chemistry research in the areas of synthetic organic chemistry, biochemistry, polymer chemistry, and materials science. Catalysis, including design, synthesis, and utilization, computational chemistry, and process modeling, are other areas in which Green Chemistry research is being conducted. An emerging area of increasing importance in Green Chemistry is that of analytical chemistry and all of its associated activities.

III. ANALYTICAL CHEMISTRY AND THE ENVIRONMENT

Analytical chemistry has been at the center of the environmental movement since the 1960s. In many different areas, the progress and activities of environmental protection has been inextricably linked to the developments and advances of analytical chemistry. Such important issues as stratospheric ozone depletion, persistent organic pollutants, and SOx and NOx air pollution were only able to be identified due to the expertise in the area of analytical chemistry. Analytical methodologies and standards are the basis for how to protect the air and water in the U.S. regulatory approaches to environmental protection. The characterization and understanding of the fate of chemicals and their metabolites as they travel from medium to medium in the environment is only possible due to the modern techniques in analytical chemistry.

As the environment movement has evolved and continues to evolve, so must the crucial role of analytical chemistry. As approaches to environmental protection have moved from the command-and-control, end-of-pipe regulatory-based approaches toward a pollution prevention, front-end voluntary-based approach, analytical chemistry is going to be essential to the success of this new trend.

As mentioned above, Green Chemistry is the manifestation of using chemistry to achieve pollution prevention. Defined as "the design of chemical products and chemical processes that reduce or eliminate the use and generation of hazardous substances", Green Chemistry has been widely adopted by industry and academia and government throughout the world. In many of the scientific innovations taking place in the area of Green Chemistry, there are new synthetic transformations and pathways, environmental benign products, and solvents/reaction systems. What is now emerging is the area of Green Analytical Chemistry in both the research arena as well as commercial sector.

IV. GREEN ANALYTICAL CHEMISTRY

It is an interesting irony that would make Heisenberg proud, that in the process of measuring environmental problems the analytical chemistry methodologies used themselves contribute to further environmental problems. This is, of course, due largely to the quantities of hazardous substances that are used in all stages of the chemical analysis life-cycle (Figure 1). From sample collection, to preparation, analysis, and disposal, the use and generation of hazardous substances are important issues. These issue go beyond concerns for laboratory waste to include important concerns for workers safety, monitoring, and energy efficiency (Figure 2). It is for these reasons that a focus area of green analytical chemistry is emerging as the design and development of new analytical procedures that we use to generate less hazardous substances.

Another important aspect of green analytical chemistry is found in the area of process analytical chemistry. Historically, the application of environmental analysis has been targeted toward the measurement and characterization of environmental problems after they are already created (e.g., measurement of dioxins in sediments). Now, there is a fairly recent focus on using the technology and expertise in process analytical chemistry to prevent pollution at the source.

Through the development and utilization of real-time, in-process sensors, the users of these

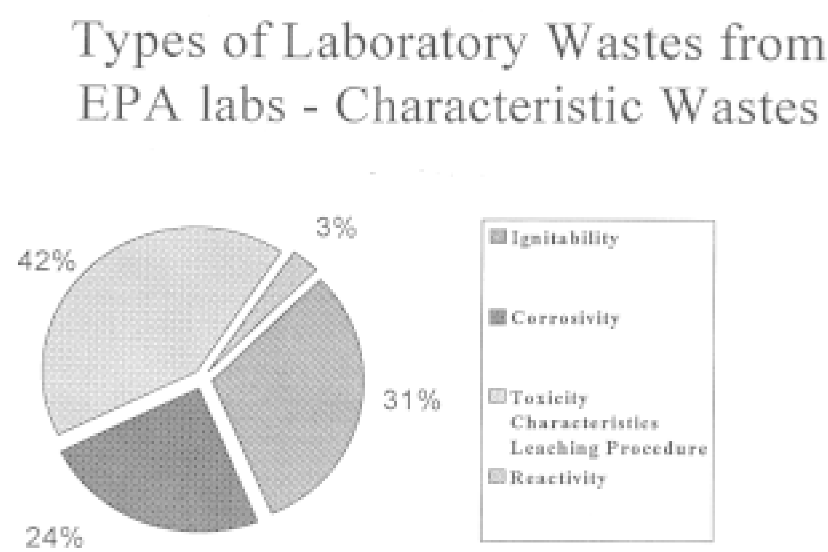

FIGURE 1

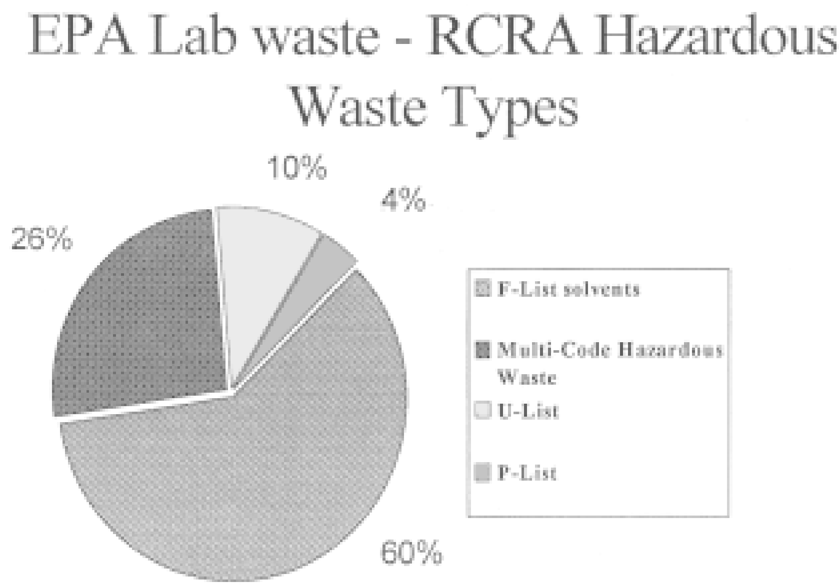

FIGURE 2

techniques can detect the formation of a hazardous substance in a manner that allows for stopping the production of undesirable substances at trace levels. Therefore, if toxic substances are being generated because of excessive heat, pressure or due to overaddition of a reactant in a manufacturing process, then the analytical sensors can adjust process parameters accordingly. In this way, pollution prevention is realized through green analytical chemistry.

V. TYPES OF GREEN CHEMISTRY IN ANALYTICAL CHEMISTRY

A. Methodology Development

New analytic methodologies are currently under development for a variety of reasons, including but not limited to:

- Economic Profile
- Increased Throughput
- Accuracy
- Efficiency
- Sensitivity

The United States Environmental Protection Agency has a collection of over 3500 methods that address over 4000 analyses in various water analytes (drinking water, waste water, etc.). So the reason for the development of new analytical methodologies are plentiful. More importantly, the reasons for the development of new methodologies are going to determine the performance criteria by which these methodologies are judged. Therefore, if the driving motivation for developing a new analytical methodology is to get an increase in the selectivity than the evaluative performance criteria will be for selectivity, primarily. In this way it is necessary to recognize that the environmental impact and the degree to which a new analytical methodology is pollution preventing must be considered as a performance criterion for any method. This is a relatively new systematic consideration in green analytical chemistry to focus on environmental performance.

With this as a focus area we can see that examples of green analytical methods are being developed and implemented throughout the analytical lifecycle. Examples of new approaches include all elements of the analytical lifecycle shown below:

- Field Analysis
- Screening
- Extraction
- Dilution Methods
- Digestion Methods
- Alternative Mobile Phase

A few of these new areas of development are discussed.

VI. FIELD ANALYSIS

The benefit of using field analysis to reduce environmental impact of traditional chemical analysis are severalfold. While there are related benefits to efficiency and financial profile, the green analytical chemistry advantages center on reducing and eliminating the use and generation of hazardous substances. Field analysis techniques (e.g., XRF) allow for the full analysis and data collection to be conducted on-site with little or no hazardous substance use.

In certain cases all requests and solvents can be eliminated from the sample collection, preparation, and analysis steps. In addition, associated advantages of reduced sample handling, transport, waste minimization, and throughput advantages result from the use of field analysis.

A particular type of field analysis that is showing particular promise for the purposes of Green Chemistry is the area of approach to chemical process, analysis, is taken off-line and analyzed in a distant laboratory far from the sampling site. Process analytical chemistry is aimed at placing the analysis at, or in-line, in the chemical process.[24] By developing these real-time, in process techniques, it is possible to detect the formation of byproducts, side-products that be hazardous, toxic, or otherwise undesirable while they are still in trace amounts. Rather than having to wait until the process is completed and having to deal with the resulting waste or off-spec materials, PAC allows for changes in the process parameters to minimize or avoid the further generation of these undesirable substances. This approach has advantages certainly for pollution prevention but also for product quality by allowing the minimization of impurities. It has benefits as well for the reduction of separations and purification because a cleaner product is being generated.

VII. SCREENING

It was often the practice in environmental analytical chemistry that in order to fully characterize a site or assess an environmental problem, there was a need to systematically test all elements of the analytical target equally. Screening methodologies have been in development for years that rely on statistical analysis and chemometric analysis to ensure validity to the approaches. These screening techniques can reduce the number of full samples throughput an analysis, considerably reducing not only time and money but also environmental damage through the use, disposal, and/or release of hazardous substances associated with the analysis.

VIII. DILUTION METHODS

Many methodologies for environmental analysis require the dilution of standards, samples, etc. Historically, this has involved the analytical chemist to visually prepare standards that are often very low in concentration for particular analytes. This has required small amounts of analyte to be diluted in large amounts of solvent. Because of human limitations in dealing with very small quantities, historically it has been the case that large amounts of either standard or sample solutions have been generated that are often orders of magnitude in volume more than is needed for their analytical purpose. Obviously, this results in considerable waste generation.

An alternative that is developing is the automation of dilutions specifically for very low concentration solutions. By having these dilutions done in an automated fashion, one can generate extremely dilute solutions in very small quantities. In this way, one can understand that large quantities of solvents for standard or sample prep can be dealt with and avoided through automated dilution.

IX. SAMPLING/SAMPLE PREP/ ANALYTICAL TECHNIQUES WITH GREEN CHEMISTRY ADVANTAGES

Specific technologies in analytical chemistry have been investigated to accomplish Green Chemistry goals. Others have been developed to meet the variety of drivers that motivate method development but yet have significant Green Chemistry benefits. A brief listing of some of the notable methods that can be used to achieve Green Chemistry goals is shown below.

- Solid-phase extraction
- Pressurized Fluid Extraction
- Micro liquid-liquid extraction
- Immunoassay techniques
- Ultrasonic extraction
- Solid-phase micro-extraction (SPME)
- X-ray fluorescence for multi-metals
- Supercritical fluid extraction
- Automated Soxhlet extraction
- Micro-extraction techniques
- Vacuum distillation of VOCs
- Membrane introduction mass spectrometry (MIMS)
- Surface acoustic wave (SAW) detection for VOCs

X. GREEN ANALYTICAL CHEMISTRY EXAMPLES

Certain technologies that have Green Chemistry advantages to them have reached a stage of development where they are either accepted or draft EPA Methods or are in widespread use for other other applications. A brief portrayal of some of these advantages for three examples is provided below.

A. Example 1

Extraction and Analysis of PCBs in Soil by Supercritical Fluid Extraction and Immunoassay (Method 2C.1) Alternative method for Soxhlet extraction and GC/ECD analysis
Green Chemistry advantages:

- Chemical usage: minimal amounts of methanol (20 ml) and microliter quantities of reaction solutions, carbon dioxide, and dilute sulfuric acid.
- Performance: detection limits of 0.02 mg/kg; accuracy of 92%; precision of 8% RSD.
- Energy usage: relatively low, SFE conducted at 100° C for 20 min; immunoassay at 25°C.

Health/safety concerns:
Using SFE at elevated pressures

B. Example 2

Extraction of Pesticides in Soil by Pressurized Fluid Extraction (EPA Method 3545)
Green Chemistry advantages

- Alternative method for Soxhlet extraction.
- Chemical usage: over 95% less solvent needed for extraction.
- Performance: comparable to established method (except for sample size limitations).
- Process: 10 min vs. 16 h for Soxhlet.
- Energy usage: 100°C for 10 min vs. hotplate for 16 h.
- Reduced exposure due to time and volume reductions.

C. Example 3

Multi-metals Analysis of Soil by XRF
(Draft EPA Method 6200) *Alternative for hotplate acid digestion / ICP-AES analysis*
Green Chemistry advantages:

- Chemical usage: none (non-destructive test)—no acid digestion needed.
- Energy usage: minimal (uses rechargeable battery).
- Accuracy: 61 to 198% (by element).
- Precision: 10 to 37% (s).
- Detection limits: 10 to 150 mg/kg.

Safety/health concerns:
Radiation exposure monitoring

These are illustrative examples that demonstrate the potential of new green analytical methodologies of accomplishing the mission of measuring, monitoring, or characterizing environmental conditions, without contributing to further environmental damage through the use and release of hazardous substances.

XI. CONCLUSION

The use of Green Chemistry principles in the design of new analytical methodologies and techniques is essential to reducing the environmental impact of environmental analytical chemistry. The same type of ingenuity and innovative tradition that has marked the area of analytical chemistry historically and allowed it to achieve remarkable goals of sensitivity, precision, and throughput is now being used to achieve the goals of reducing or eliminate the use and generation of hazardous substances in environmental analysis.

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