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Green Chemistry: Hope-Not Hype, Promise-Not Peril

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ABSTRACT:
In this analysis we havefocused on the science that elucidates the principles of Green Chemistry, in particular the profitable use of materials and energy, development of sustainable resources, and layout for diminished hazards. Green Chemistry has immense indications for energy and the environment. As the chemical industry forthwith accounts for a momentous portion of energy exhaust by the manufacturing sector, Acceleration in catalysis and substitution to conventional heating in chemical processes will play a crucial role in establishing the sustainability of the chemical business.

Introduction

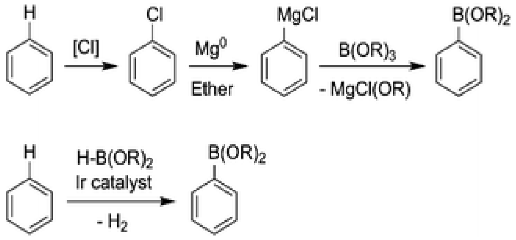
The scientific question facing the chemical sector when designing for the future earth is not whether products of the chemical industry will be necessary, because they surely will be.(1) Over the past two decades, the movement of green chemistry has become a new standard embraced for the development of less harmful materials & chemicals that are safer for both the environment & consumers. (2)

The twelve principles of green chemistry as outlined by Anastas& Warner and presented by Tang et. Al (3)are(4)

- Prevention of waste
- Atom economy
- Less hazardous chemical synthesis
- Designing safer chemicals
- Safer solvents & auxiliaries
- Design for degradation
- Real-time analysis for pollution prevention
- Inherently safer benign chemistry for accident prevention
- Reduce derivatives
- Use of renewable feedstock
- Catalysis (vs. Stoichiometric)
- Design for energy efficiency

Green chemistry practice has been adopted into mainstream research & manufacturing since the early 1990s. Success stories of the application & study of green chemistry include the case of microbes as environmentally benign synthetic catalysts (5-7). A complementary tool for green chemistry & green engineering that incorporates the toxicological risk & hazard assessment of the design to disposal of products & material is the concept of green toxicology (8). With new technologies becoming more readily available, we are now at a point where there is a chance to tackle complex toxicological concern, such as synthetic toxicity(9)

As the green chemistry movement has gained momentum, definitions of green chemistry have been dominated predominantly by academic view point. Green chemistry concept, however, applies to an incredible diversity of scientific endeavor, which has invariably led to differences between & amongst both academia & industry regarding what constitutes green chemistry.(10)



Richard F. Heck and Ei-Ichi Negishi, were awarded in September 2010, the Nobel Prize in Chemistry

for "palladium-catalyzed cross couplings in organic synthesis". Early Suzuki coupling was waste intensive; a typical synthesis might require reaction of an aryl chloride with a Grignard reagent followed by addition of a trialkyl borate ester generating stoichiometric magnesium chloride & alkoxide waste, in addition to any waste associated with preparing the chlorinated feedback. The award winning chemistry is halogen – free, based on thermal, catalytic activation of an aryl carbon hydrogen bond. The only co-product is hydrogen. The iridium catalysis is robust & selective, allowing some synthesis to be carried out in solvent free condition. (12)

Green Chemistry has also aimed to eliminate waste caused by catalysts themselves, including metal, solvent, and auxiliary waste generated in catalyst quenching and separation processes. Many strategies have been developed to improve catalyst recyclability. Immobilization of catalysts on inorganic polymers supports facilitates catalyst recovery and regeneration and minimizes contamination of products. Catalysts have also been designed with properties that allow them to be readily recovered by adjusting pH or temperature (13)

Nature is the source of inspiration for new catalytic chemistry. Modelling of enzyme active sites has led to the development of first-row transition metal complexes with simple ligands that can carry out enzyme-like transformations. For example, non-heme iron oxygenases were the inspiration for the first iron catalysts to activate H_2O_2 to carry out stereo specific oxidation of alkanes (14)

Designing safer chemical processes

The future of green chemistry requires that chemists take on a more proactive role in designing processes for reduced hazard, to avoid the kind of cycle that leads to accidental environmental damage, toxicity surprises, and daunting cleanup problems: (15-16)

Green chemistry can entail many things-

1. A chemist synthesizes a novel chemical.
2. The chemical enters commerce and is dispersed around the world.
3. Alarms are sounded about persistence, bioaccumulation, toxicity, etc.
4. Legislation bans or restricts further use; remediation programs are implemented.
5. A novel chemical is required to replace the previous offender.

It will be necessary for chemists to relate molecular structure not only to intended function, but also unintended behavior: mobility, persistence, and fate in humans, animals, and the environment. It has been proposed that design rules should be established based on (in order of importance) (17-18)

1. Molecular toxicology that relates structural features to mechanisms of action.
   a. Avoidance of toxic chemical classes or functional groups.
   b. Structural blocking or relocation of toxic groups.
2. Quantitative structure-activity relationships (QSARs) that predict potential hazards when mechanistic data is unavailable.
3. Toxicokinetics and toxicodynamics studies to ensure safe metabolism.
   a. Planned biochemical elimination of toxic groups.
   b. Facilitation of excretion.
   c. Facilitation of biodegradation.
4. Decreasing bioavailability so that a chemical released into the environment cannot pass through relevant biological barriers.
   a. Appropriate molecular size.
   b. Low volatility.
   c. Appropriate water solubility and lipophilicity.
   d. Consideration of specific routes of absorption.

The future of designing safer chemicals will most likely be linked to developments in toxicogenomics and other "omics" fields. Toxicogenomics is the study of the effect of a toxin on the expression of genes on the cell level. The patterns of gene expression offer "fingerprints" for different kinds of toxicological responses, allowing chemicals to be classed according to the kind of biological damage they are capable of. Toxicogenomic information can be supplemented by proteomics (patterns of protein expression) and metabolomics/metabonomics (changes in levels of metabolites). (19

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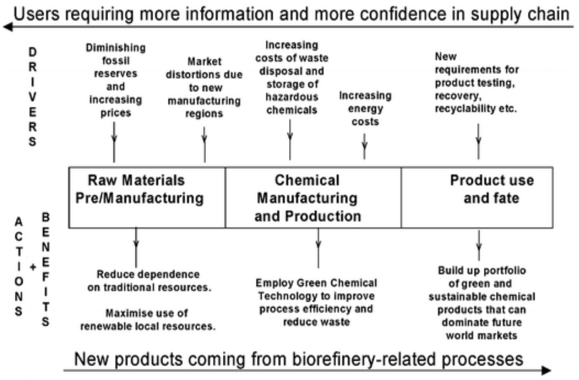
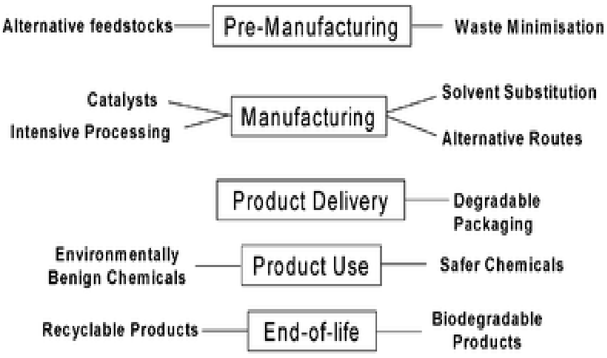
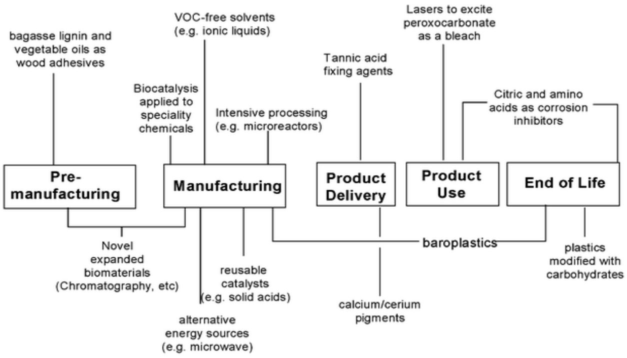
Green Chemistry and Tomorrow



As the economic opportunities for greener products become more apparent, so should this process of product greening accelerate and in an ideal situation, iterative innovation to improve the environmental performance of chemical products will become continuous and embedded in industry's philosophy. Now is the time as the drivers come into effect to ensure that this process is indeed sustainable by never losing sight of the lifecycle of any chemical product. (20)

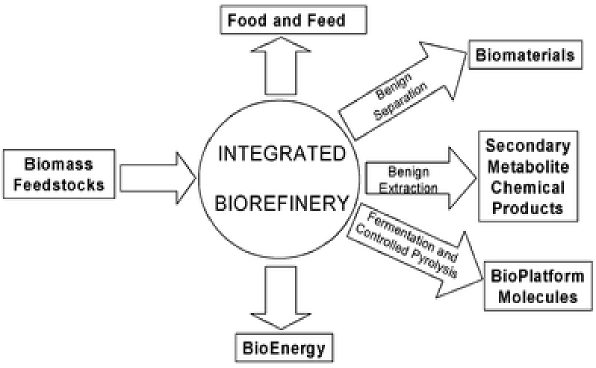


Some examples of recent progress in Green Chemistry

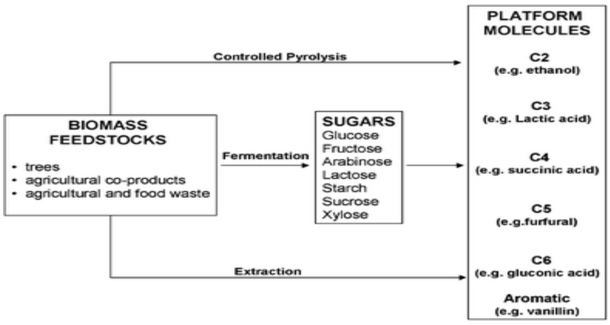


Our own efforts to engage the producers and retailers as well as the users of products containing chemicals in the green chemistry networks project, "Green Chemistry and the Consumer", has made us aware of the very small amount of relevant research reported in the mainstream chemistry journals (21)

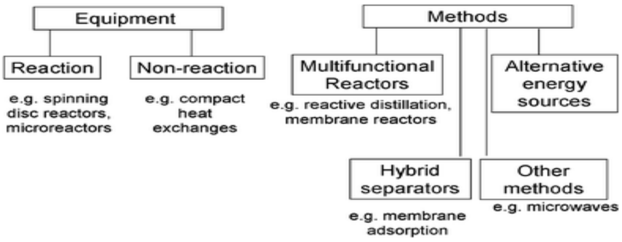
Green chemistry in bio refinery



Bio platform molecules



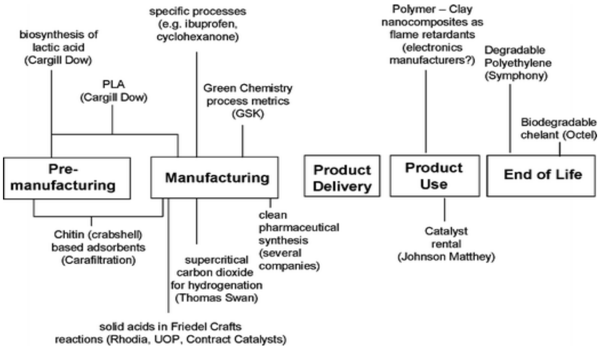
Process intensification



The green chemistry process research on novel catalysts, benign (non-VOC) solvents, *etc.* is now being strengthened and moved closer to industrial application through the innovative contributions from chemical and process engineers, notably in the context of process intensification—scale out, not up.

Examples of Green Chemistry at Present

The growth in industrial utilization of new, greener technologies in recent years is encouraging though it still only represents a tiny fraction of the total volume of chemical manufacturing worldwide. Interesting case studies are now available at all stages in the life cycle.



The last 7 years have also seen a very welcoming growth in the number of green chemistry centers, initiatives and networks across the world. In many cases local activities have started with a very appropriate blend of education and research, reflecting the trend in the more established networks such as the GCN and the GCI(22-23)

Green chemistry & Human health

The following are the examples of approaches that make use of *in vitro* data in human health assessments that also are useful with respect to assessments of alternatives:

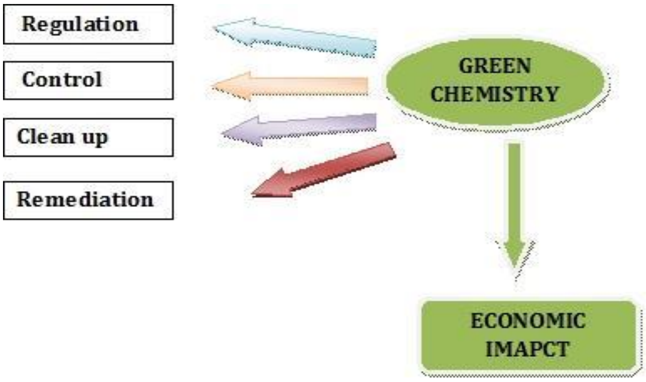
1. **Crump et al. (2010)** argued that *in vitro* data can be used in ways similar to the current process of risk assessment, except that additional safety factors may need to be applied to account for extrapolation from *in vitro* to *in vivo*. The authors also argued that pathways-based models of toxicity **(National Research Council, 2007)** may not be useful for quantitative decision-making. The statistical variability inherent in complex models may hinder their ultimate utility for estimating small changes in response. Furthermore, such models involve empirical modeling of dose-responses.
2. **Judson et al. (2011)** proposed using *in vitro* data and pharmacokinetic models, coupled with estimates of population variability and uncertainty, to estimate the human dose at which a chemical may significantly alter a biological pathway *in vivo*, a so called biological pathway altering dose. This approach draws parallels between a chemical-associated perturbation of a pathway as observed in *in vitro* assays and a key event in the chemical's mode of action that may lead to an adverse health outcome. This approach offers an opportunity to not only compare alternatives with regards to the potential of human health hazard, but also take into account
the quantitative and variability aspects of the underlying adverse effects.
3. **Thomas et al. (2013)** reasoned for a step-wise decision tree that incorporates *in vitro* assays, toxicokinetic modeling and short-term animal data into toxicity testing and risk assessment in an integrated fashion. Tier I of this approach informs the use of *in vitro* data in chemical alternative assessment. This phase uses *in vitro* assays to rank chemicals based on their relative selectivity in interacting with biological targets that have been associated with known toxicityoutcomes and to identify the concentration at which these effects occur. Reverse toxicokinetic modeling and *in vitro*-to *in vivo* extrapolation modeling **(Wetmore, 2015)** can then beused to convert *in vitro* concentrations into external doses for derivation of the point-of-departure values. The latter can be compared with human exposure data or estimates **(Wambaugh et al., 2013)** to yield a margin of exposure.
4. The use of toxicokinetic information as a sufficient consideration in and of itself to enable rapid decisions on the risk of chemicals has been extended by **Wambaugh et al. (2015)** through the proposal for high-

throughput physiologically based toxicokinetic model that predicts nonsteady-state chemical concentration time-courses for a variety of exposure scenarios. The authors used this model to propose a 4-element framework for chemical toxicokinetic triage thatcan group chemicals into categories based on varying levels of confidence in predictions of exposure, an approach that may be useful for triaging chemicals for which high throughputtoxicokinetic predictions may be sufficient, and identifying those that may require additional experiments to collect appropriate data.

5. The U.S. EPA's advancing the Next Generation of Risk Assessment program **(Cote et al., 2016)** considered options for how novel biological data and methods could better inform decision-making. New data and methods including transcriptomics, genomics, and proteomics; methods included molecular epidemiology and clinical studies, bioinformatics knowledge mining, pathway and network analyses, short-duration *in vivo* and *in vitro* bioassays, and quantitativestructure activity relationship (QSAR) modeling were applied and evaluated for use in hazard identification and dose response assessment. It was concluded that considerable uncertainties notwithstanding, application of new knowledge to risk assessment is warranted for the whole spectrum of decision contexts, from major scope assessments to prioritization and screening of very data limited chemicals.

6. The use of the *in vitro* and other novel data in the framework of the Adverse Outcome Pathway (AOP) is gaining interest with respect to decision-making applications **(Edwards et al., 2016).** The AOP concept has been proposed by the Organization for Economic Cooperation and Development (OECD) as a vehicle for linking the molecular screening and mechanistic toxicology data to *in vivo* adverse events of interest in human health and environmental assessments by describing a sequential progression from the chemical to the molecular initiating event, to the cellular, organ, organism and population response that underlies the *in vivo* outcome of interest **(OECD, 2017).** The overarching goal in using AOPs is to reduce the uncertainty in decision-making by identifying key intermediate events and quantitatively linking them to final adverse outcomes relevant to risk assessment. AOP framework provides transparency, allows for assessment of mechanistic probability, and enables hypothesis-based and decision context-relevant *in vitro* and *in silico* testing of a large number of chemicals. Conceptually, the AOP framework may therefore be very useful to definea set of"adverse outcomes" that can be identified, e.g., the types of adverse human health effects that are traditionally used in making "alternatives" or "design" chemical hazard assessmentdecisions.

Hazard identification relies on multiple data streams. These include human epidemiologic or experimental studies, animal bioassays, and increasingly numerous *in vitro* and *in silico* novel assessment methodologies (Rusyn and Daston, 2010). The National Academies reports of Toxicity Testing in the 21st Century (TT21C): A Vision and a Strategy (National Research Council, 2007) and Using 21st Century Science to Improve Risk-Based Evaluations (National Academies of Sciences, 2017) endorsed the use of novel assessment methodologies in decision-making. Similarly, advances in chemistry and material sciences create new opportunities for more green chemistry and use of alternative materials in products and processes.



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Education with Green Chemistry

Both the environmental protection agency (EPA) and American chemical agency (ACS) have recognized the importance of bringing Green chemistry to the classroom and the laboratory.

Some suggestions are (25)

1- Organizing an interdisciplinary green chemistry workshop on campus
2- Working with a local company on a green chemistry project
3- Developing a green chemistry activity with a local school
4- Converting a current laboratory experiment into a greener one
5- Organizing a green chemistry poster session on campus
6- Distributing a green chemistry newsletter to the local community
7- Designing a green chemistry web page

In Developing countries, the introduction of green chemistry is still in a stage of infancy, despite the significant need and the significant role green chemistry can play. Many of the practices in developing countries are still far from the concept of safety, pollution prevention and design of energy efficiency.

Green chemistry in Daily Life

1. Dry Cleaning of Clothes

Perchloroethylene (PERC), $Cl_2C=CCl_2$ is commonly being used as a solvent for dry cleaning. It is now known that PERC contaminates groundwater and is a suspected carcinogen. A technology, Known as Micelle Technology developed by Joseph De Simons, Timothy Romark, and James McClain made use of liquid CO_2 and a surfactant for dry cleaning clothes, thereby replacing PERC. Dry cleaning machines have now been developed using this technique. Micelle Technology has also evolved a metal cleaning system that uses CO_2 and a surfactant, thereby eliminating the need of halogenated solvents(26).

2. Versatile Bleaching Agents

It is a common knowledge that paper is manufactured from wood (which contains about 70% polysaccharides and about 30% lignin). For good quality paper, the lignin must be completely removed. Initially, lignin is removed by placing small chipped pieces of wood into a bath of sodium hydroxide (NaOH) and sodium sulphide (Na_2S) [that is how pulp is formed]. By this process about 80-90% of lignin is decomposed. The remaining lignin was so far removed through reaction with chlorine gas (Cl_2). The use of chlorine removes all the lignin (to give good quality white paper) but causes environmental problems. Chlorine also reacts with aromatic rings of the lignin (by aromatic substitution) to produce dioxins, such as 2,3,4-tetrachloro-dioxin and chlorinated furans. These compounds are potential carcinogens and cause other health problems. Other bleaching agents like hydrogen peroxide (H_2O_2), ozone (O_3) or oxygen (O_2) also did not give this the desired results. A versatile agent has been developed by Terrence Collins of Camegie Mellon University. It involves the use of hydrogen peroxide as a bleaching agent in the presence of some activators known as TAML activatorsthat act as catalysts which promote the conversion of hydrogen peroxide into hydroxyl radicals that are involved in oxidation/ bleaching. The catalytic activity of TAML activators allows hydrogen peroxide to break down more lignin in a shorter time and at much lower temperature. These bleaching agents find use in laundry and result in lesser use of water.

Current status

Since 1991, Green Chemistry has grown into a significantly internationally engaged focus area within chemistry.Research has focused on both, the micro and molecular levels .The carbohydrate economy provides a rich source of feedstock for synthesizing commodities(27).

(i) A continuous process and apparatus converts waste biomass into industrial chemicals, fuels and animal feed. Another process converts waste biomass such as municipal solid waste, sewage sludge, plastic, tires and agricultural residues to useful products, including hydrogen, ethanol and acetic acid.

(ii) A fermentation method for the production of carboxylic acids.Shells from crabs and other sea life serve as a valuable and plentiful source of chitin, which can be processed into chitosan, a biopolymer with a wide range of potential applications that are being currently explored for use in the oil-drilling industry (28).

(iii) A method for mass producing taxol by semi continuous culture of Taxus genus plant.

(iv) The first bio-pesticide for sugarcane, called Bio Cane, has recently been launched in Australia. The product is based on a naturally-occurring fungus that has been cultured on broken rice grains to provide a medium for distribution. Biocane granules are claimed to be particularly effective against greyback cane grub.

(v) Genetic engineering produces valuable chemical products via non-traditional pathways.

(vi) Glucose Yields Catechol and adipic acid (29).

(vii) Saccharomyces yeasts convert both glucose and xylose, present in cellulogic biomass, into ethanol (29).

(viii) A new environmentally friendly technology in mixed metals recovery from spent acid wastes has been used to recover zinc and ferrous chloride from pickle liquor.

(ix) CO_2 is also a renewable feedstock that has been incorporated into polymers (30).

(x) A method of partially oxidizing alcohol such as methanol to ethers, aldehydes, esters or acids, by using a supercritical fluid mobile.

(xi) The demand for non-ionic surfactants is growing and a new example of this is alkyl glycoside, which is made from saccharide. This product can be used as a replacement for alkylarylsulfonate anionic surfactants in shampoos. Sodium silicate can be used as a more environmentally benign replacement for phosphorus-containing additives in washing powder. Three coconut oil soap bases for liquid cleansing applications have been developed. One of these products has a very light color and low odor, making it suitable for introducing dyes and fragrances. Chemistry for achieving environmental and economic prosperity is inherent in a sustainable world. One important element of sustainable chemistry is commonly defined as the chemical research aiming at the optimization of chemical processes and products with respect to energy and material consumption, inherent safety,toxicity, environmental degradability, and so on. (31)

Green chemistry: Economy and business (32)

- Higher yields for chemical reactions, consuming small amounts of feedstock to obtain the same amount of product
- Fewer synthetic steps, often allowing faster manufacturing of products, increasing plant capacity, and saving energy and water
- Reduced waste, eliminating costly remediation, hazardous waste disposal, and end-of-the-pipe treatments
- Allow replacement of a purchased feedstock by a waste product
- Better performance so that less product is needed to achieve the same function
- Reduced use of petroleum products, slowing their depletion and avoiding their hazards and price fluctuations
- Reduced manufacturing plant size or footprint through increased throughput
- Increased consumer sales by earning and displaying a safer-product label (e.g., Safer Choice labeling)
- Improved competitiveness of chemical manufacturers and their customers

Conclusion

The expansion of green chemistry over the course of the past decades needs to increase at an accelerated pace if molecular science is to meet challenges of sustainability. Most importantly we need the relevant scientific, engineering, educational and other communities to work together for a sustainable future through green chemistry.

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