



## Green Chemistry: A New Approach to The Synthesis, Processing and Application of Chemical Substances

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### Abstract

Issues in the past decade demonstrate many methodologies that protect human health and the environment in an economically beneficial manner that is green chemistry. The beginning of green chemistry is frequently considered as a response to the need to reduce the damage of the environment by man-made materials and the processes used to produce them. In the present study the implementation of green chemistry principles in everyday life in industry, the laboratory and in education are concluded. A brief introduction of green chemistry and future prospects are also mentioned. Green Chemistry is a new approach to the synthesis, processing and application of chemical substances, thus diminishing the hazards for human health and environmental pollution. Anastas proposed twelve principal of green chemistry which are more valuable and help to prevent environmental pollution and make it ecofriendly. Some precaution should considered during lab work like close fume hood when do not use, run experiment on micro scale to reduce waste etc. Green chemistry also become a valuable tool for the day to day life by using green dry cleaning of clothes ( use of Perchloroethylene replace by liquid CO<sub>2</sub>), versatile uses of green bleaching agents as H<sub>2</sub>O<sub>2</sub>, Green solution to turn turbid water clears, production of biodiesel etc. Some important tools used in the synthesis of drug and chemicals which are proved as ecofriendly as microwave assisted synthesis, dry media organic synthesis reaction , computer aided drug designing, use of green solvents , use of green catalyst etc

**Keywords:** Green Chemistry, Ecofriendly, Microwave Synthesis, Green Solvents

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### Introduction

The term “Green Chemistry” was introduced for the first time by Anastas in 1991 in a special program created by the US Environmental Protection Agency (EPA) in order to stimulate a substantial development in chemistry and chemical technology. [1,2] Green Chemistry comprises a new approach to the synthesis, processing and application of chemical substances, thus diminishing the hazards for human health and environmental pollution.[3] Green Chemistry may prove a valuable tool to promote innovative chemical technologies that reduce or eliminate the use or generation of hazardous substances in the design, manufacture and use of chemical products.[4] Progress

in science and technology in the second half of the twentieth century has led to significant economic development and an increase in living standards in developed parts of the world.[5] Many forward-looking companies are embracing Green Chemistry, not only to protect the environment and to create good public relations, but also because it is often beneficial to the bottom line. According to a data available, it is also estimated to cost US industries between \$ 100 and \$ 150 billion per year to comply to environmental regulations.[6] Among the greatest achievements of green chemistry, are petrochemical and pharmaceutical industries. But these industries are often blamed for polluting environment. The challenge for the present-day chemical industry is to continue providing applications and socioeconomic benefits in an environmentally friendly manner that can be achieved by green chemistry.[7]

### Principles of green chemistry

There are total of twelve principles contributing the green chemistry. These are elaborated as follows:

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

**Atom Economy:** Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.

**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.

**Designing Safer Chemicals:** Chemical products should be designed to affect their desired function while minimizing their toxicity.

**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.

**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.

**Use of Renewable Feed stocks:** A raw material or feedstock should be renewable rather than depleting whenever technically and economically practicable.

**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.

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

**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.

**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.

**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.<sup>[8]</sup>

### Green chemistry in day-to-day life

**Green Dry Cleaning of Clothes:** Perchloroethylene (PERC) is commonly being used as a solvent for dry cleaning. It is now known that PERC which contaminates ground water and is a suspected carcinogen. A technology, known as Micell technology developed by Joseph De Simons, Timothy Romark, and James McClain made use of liquid CO<sub>2</sub> and a surfactant for dry cleaning clothes, thereby replacing PERC. Dry cleaning machines have now been developed using this technique. Micell Technology has also evolved a metal cleaning system that uses CO<sub>2</sub> and a surfactant thereby eliminating the need of halogenated solvents.<sup>[9]</sup>

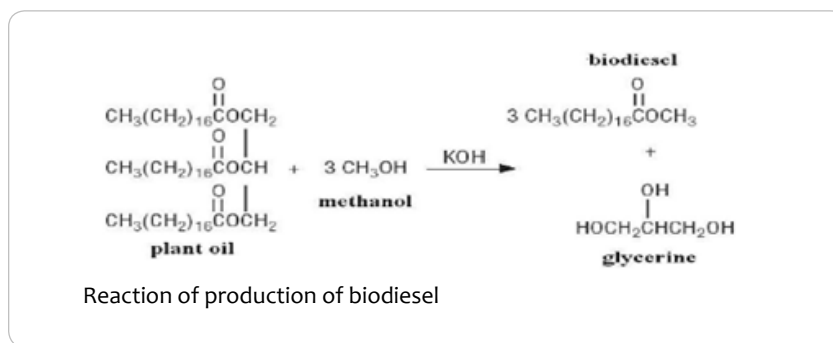
**Versatile Bleaching Agents:** It is common knowledge that paper is manufactured from wood (which contains about 70% polysaccharides and about 30% lignin). For good quality paper, the lignin must be completely removed. Initially, lignin is removed by placing small chipped pieces wood into a bath of sodium hydroxide (NaOH) and sodium sulphide (Na<sub>2</sub>S). By this process about 80-90% of lignin is decomposed. The remaining lignin was so far removed through reaction with chlorine gas (Cl<sub>2</sub>). 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 to

produce dioxins, such as 2,3,4-tetrachlorodioxin and chlorinated furans. These compounds are potential carcinogens and cause other health problems. These halogenated products find their way into the food chain and finally into products, pork, beef and fish. A versatile agent has been developed by Terrence Collins of Carnegie Mellon University. It involves the use of H<sub>2</sub>O<sub>2</sub> as a bleaching agent in the presence of some activators known as TAML activators,<sup>[10]</sup> that as catalysts which promote the conversion of H<sub>2</sub>O<sub>2</sub> into hydroxyl radicals that are involved in oxidation (bleaching). The catalytic of TAML activators allow H<sub>2</sub>O<sub>2</sub> to break down more lignin in a shorter time and at much lower temperature. These bleaching agents find use in laundry and results in lesser use of water.<sup>[11]</sup>

**Green Solution to Turn Turbid Water Clear:** Tamarind seed kernel powder, discarded as agriculture waste, is an effective agent to make municipal and industrial waste water clear. The present practice is to use Al-salt to treat such water. It has been found that alum increases toxic ions in treated water and could cause diseases like Alzheimer's. On the other hand kernel powder is not-toxic and is biodegradable and cost effective. For the study, four flocculants namely tamarind seed, kernel powder, mix of the powder and starch, starch and alum were employed. Flocculants with which slurries were prepared by mixing measured amount of clay and water. The result showed aggregation of the powder and suspended particles were more porous and allowed water to ooze out and become compact more easily and formed larger volume of clear water. Starch flocks on the other hand were found to be light weight and less porous and therefore didn't allow water to pass through it easily. The study establishes the powder's potential as an economic flocculants with performance close more established flocculants such as K<sub>2</sub>SO<sub>4</sub>Al<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>·24H<sub>2</sub>O (potash alum).<sup>[12]</sup>

**Production of adipic acid:** Large amounts of adipic acid are used each year for the production of nylon, polyurethanes and lubricant sand plasticizers. Benzene (a compound with carcinogenic properties) is a standard substrate for the production of this acid. Chemists from State University of Michigan developed green synthesis of adipic acid using a less toxic substrate. Furthermore, the natural source of this raw material, glucose is almost inexhaustible. The glucose can be converted into adipic acid by an enzyme discovered in genetically modified bacteria. Such a manner of production of these acid guards the workers and the environment from exposure to hazardous chemical compounds.<sup>[13]</sup>

**Production of biodiesel:** Many vehicles around the world are fueled with diesel oil which is a well known pollutant and the production of biodiesel oil is a promising possibility to be eco friendly. As the name indicates, biodiesel oil is produced from cultivated plants oil, e.g. from soya beans. It is synthesized from fats embedded in plant oils by removing the glycerin molecule. The advantages of using biodiesel oil are obvious. It's fuel from renewable resources and contrary to normal diesel oil.<sup>[14]</sup>



## Role of green chemistry in synthesis of drugs and chemicals to make ecofriendly

**Microwave synthesis:** Microwave assisted organic synthesis has revolutionized organic synthesis. Small molecules can be built in a fraction of the time required by classical thermal methods. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes. A microwave is a form of electromagnetic energy, which falls at the lower end of the electromagnetic spectrum and is defined in a measurement of frequency as 300 to 300,000 Megahertz, corresponding to wavelengths of 1 cm to 1 m. The microwave region of the electromagnetic spectrum lies between infrared and radio frequencies.<sup>[15,16]</sup> Historically, chemists thought that compounds react only in the liquid state or if dissolved.<sup>[17]</sup> This has made solvents common in chemical syntheses, however, many compounds used as solvents were found to be environmentally unfriendly. The problem associated with waste disposal of solvents has been overcome by performing reactions without a solvent under microwave irradiation (MWI).<sup>[18]</sup> Coupling of MWI with the use of mineral-supported catalyzed reactions, under solvent-free conditions, provides clean chemical processes with the advantage of enhanced reaction rates, higher yields, greater selectivity, and greater ease of

manipulation. These expeditious and solvent-free approaches involve the exposure of neat reactants to MWI in conjunction with the use of supported reagents or catalysts.<sup>[19]</sup>

Dry media reactions in organic synthesis by microwave -Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient, and economical technology (green chemistry). There is an increasing interest in the use of environmentally benign reagents and procedures. Or, in other words, the absence of solvents coupled with the high yields and short reaction times often associated with reactions of this type make these procedures very attractive for synthesis. In the present discussion, we describe the advantages of dry reaction techniques coupled with microwave activation and their applications to organic synthesis using solid supports. The practical dimension to the microwave heating protocols has been added by accomplishing reactions on solid supports under solvent-free conditions.<sup>[20]</sup> These solvent-free microwave-assisted reactions<sup>[21]</sup> provide an opportunity to work with open vessels, thus avoiding the risk of high-pressure development and increasing the potential of such reactions to upscale. The practical feasibility of microwave-assisted solvent-free synthesis has been demonstrated in various useful transformations<sup>[22,23]</sup> and in synthesis of heterocyclic systems.<sup>[24,25]</sup>

S.No.	Microwave assisted Reactions		
1.	Acetylation reaction	8	Elimination reaction
2.	Addition reaction	9	Estrification reaction
3.	Alkylation reaction	10	Hydrolysis reaction
4.	Alkynes metathesis	11	Halogenation reaction
5.	Allylation reaction	12	Condensation reaction
6.	Diel's-Alder reaction	13	Oxidation reaction
7.	Dimerization reaction	14	Reduction reaction

**Table 1:** Microwave Assisted Reactions

**Inorganic synthesis:** Synthesis of organometallic and coordination compounds, Synthesis of intercalation compounds, Synthesis of ceramic products etc can be contribute to green chemistry.<sup>[26,27]</sup>

### Applications in Analytical Chemistry:

**Ashing:** Microwave heating is extensively used for ashing in the petroleum and fuels, plastics, pharmaceuticals and food industries. In most of these industries, microwave powered muffle furnaces, which are specifically meant for laboratory use, are used for ashing.<sup>[28]</sup>

**Digestion:** Digestion is the process by which samples are broken down to their basic constituents for chemical analysis. Microwave digestion systems are used in analytical laboratories for sample decomposition and preparation. It involves the heating of microwave-absorbing reagents inside a pressurized, microwave-transparent container, in contrast to conventional open vessel digestion. Pressurization allows higher temperatures to be achieved in short period and it increases the speed of digestion. Rapid heating accelerates the reaction rate exponentially and results in an approximately 100-fold decrease in the time required for the process of digestion at 175 °C, compared to such a process conducted at 95 °C.

**Moisture analysis:** Application of microwave assisted moisture analysis has been extended to food and beverage, chemical, environmental, organic and pharmaceutical industries and has been found to be highly effective in reducing testing time.

**Extraction:** Microwave extraction has proved to be more effective and efficient than its conventional counterpart, the Soxhlet extraction method. The Soxhlet extraction, which is a standard technique, is a continuous solvent extraction method. Extraction systems are used to conduct routine solvent extractions of soils, sediments, sludge, polymers and plastics, pulp and paper, biological tissues, textiles and food samples. Experiments have proved that microwaves, in comparison with the Soxhlet extraction, use a lesser volume of solvent and sample and perform extraction at a much faster rate.<sup>[29]</sup>

**Computer aided drug designing:** The computational method of drug designing will be able to predict affinity before a compound is synthesized and hence in theory only one compound needs to be synthesized, saving enormous time and cost. Because of one of the compounds need to be synthesis, it reduces other compounds and intermediates during synthesing of the drug molecules. The reality

is that present computational methods are imperfect and provide, at best, only qualitatively accurate estimates of affinity. In practice it still takes several iterations of design, synthesis, and testing before an

optimal drug is discovered. Computational methods have accelerated discovery by reducing the number of iterations required and have often provided novel structures.<sup>[30,31]</sup>

Drug	Approved in year	Biological actions
Captopril	1981	Antihypertensive
Dorzolamide	1995	Carbonic anhydrase inhibitors
Indinavir	1996	Human immunodeficiency virus (HIV)
Ritonavir	1996	Human immunodeficiency virus (HIV)
Saquinavir	1995	Human immunodeficiency virus (HIV)
Triofiban	1998	Fibronogen antagonist
Raltegravir	2007	Human immunodeficiency virus (HIV)
Zanamivir	1999	Neuramidase inhibitors
Aliskiren	2007	Human renin inhibitors
Boceprevir	PhaseIII Clinical trials	Hepatitis C VIRUS (HCV) Inhibitors
Nolatrexed	PhaseIII Clinical trials	Liver cancer
TMI-005	PhaseII Clinical trials	Rheumatoid arthritis
Oseltamivir	1999	Active against influenza A and B viruses
LY-517717	PhaseII Clinical trials	Serine protease inhibitor
NVP-AUY922	PhaseI Clinical trials	Inhibitor for HSP90

Table 2: List of clinically approved drugs discovered by CADD [32]

### Solvents in pharmaceutical process development and greenness factors:

A solvent (from the Latin solvō, “loosen, untie, solve”) is a substance that dissolves a solute (a chemically distinct liquid, solid or gas), resulting in a solution. A solvent is usually a liquid but can also be a solid, a gas, or a supercritical fluid. The quantity of solute that can dissolve in a specific volume of solvent varies with temperature. Common uses for organic solvents are in dry cleaning (e.g. tetrachloroethylene), as paint thinners (e.g. toluene, turpentine), as nail polish removers and glue solvents (acetone, methyl acetate, ethyl acetate), in spot removers (e.g. hexane, petrol ether), in detergents (citrus terpenes) and in perfumes (ethanol). Water is a solvent for polar molecules and the most common solvent used by living things; all the ions and proteins in a cell are dissolved in water within a cell. Solvents find various applications in chemical, pharmaceutical, oil, and gas industries, including in chemical syntheses and purification processes. But sometime these solvents also produce harmful effects on environment and also human welfare. To overcome such kind of problems laboratories, chemical synthesis companies and pharmaceutical companies discover and research alternative methodology to use ecofriendly solvents.

Solvents have received much attention under the remit of green chemistry<sup>[33,34,35,36,37]</sup>. This can be ascribed to the large volume of solvent typically used in a reaction (especially at the purification stage) or in a formulation<sup>[38,39]</sup>. Despite this, the solvent is not directly responsible for the composition of a reaction product, nor is it the active component of a formulation. Therefore the use of toxic, flammable, or environmentally damaging solvents would seem unnecessary because these characteristics have no impact on the function or progress of the system in which the solvent is applied. However these

unfortunate consequences of solvent use are often linked to the beneficial attributes of the solvent needed for the application. The volatility of solvents permits recovery and purification of the solvent by distillation, but also creates unwanted air emissions and the risk of worker exposure. Amide solvents have the high polarity required to dissolve a broad range of substrates and accelerate reactions<sup>[40]</sup>, but this functionality often implies reproductive toxicity<sup>[41]</sup>. At the other end of the polarity scale hydrocarbon solvents provide the ability to dissolve oils in extractions and perform separations<sup>[42, 43]</sup>, yet at the same time they are highly combustible, and their low water solubility (high logP) is linked to bioaccumulation and aquatic toxicity<sup>[44, 45]</sup>.

In attempts to eliminate undesirable solvents, replacement strategies often seek structurally related compounds not yet covered by the legislative and regulatory measures usually required to force action in this respect. Thus benzene, since its formal recognition as a carcinogen in the mid-twentieth century, is generally replaced by toluene<sup>[46, 47]</sup>. Similarly the Montreal protocol has restricted the use of carbon tetrachloride since 1989 because of its role in depleting the ozone layer<sup>[48, 49]</sup>. Typically the halogenated solvents chloroform and dichloromethane (DCM) are now used instead. It is important to emphasise that these measures have proven to be short sighted with respect to increasingly strict chemical controls worldwide. Toluene is in fact suspected of damaging the unborn child and of organ damage through prolonged exposure<sup>[50, 51]</sup>. Chloroform and DCM are likely to be carcinogenic to humans according to the World Health Organization IARC evaluations. In addition to DCM, even as a short-lived halogenated substance has now been shown to be ozone depleting as well<sup>[52]</sup>.

Hazardous solvents	Issues	Green solvents (alternate solvents)
Pentane	Lower flash point than other similar solvents	Heptane
Diethyl ether	Lower flash point than other similar solvents	2-MeTHF, TEME
Diisopropyl ether	Powerful peroxide formation compared to similar solvents	2-MeTHF, TEME
Hexane	More toxic than other similar solvents	Heptane
Benzene	Carcinogen	Toluene
Chloroform	Carcinogen	DCM
1,2-DCE	Carcinogen	DCM
1,2- DME	Carcinogen	2-MeTHF, TEME
Pyridine	Carcinogenicity (not classifiable)	Triethylamine (base)
1,4- Dioxane	Carcinogenicity (not classifiable)	2-MeTHF, TEME
DCM	Emissions	Application dependent
Carbon tetrachloride	Emissions	DCM
DMF	Reproductive toxicity	Acetonitril
DMAc	Reproductive toxicity	Acetonitril
NMP	Reproductive toxicity	Acetonitril

**Table 3:** Pfizer replace various hazardous solvents with the green solvents are listed.[53]

**Use of water in organic synthesis:** Water can replace many toxic and hazardous solvents and has been found very efficient in many organic reactions. An efficient and handy method for the synthesis of chromeno-isoxazole/isoxazolines under on water conditions has been described [54]. Hydrolysis of hydrophobic glycidyl ethers in pressurized water media can afford the corresponding glyceryl ethers in good to excellent selectivity within several minutes without a catalyst [55]. Selective and efficient aerobic oxidative iodination of ketones in aqueous media has been achieved by using molecular iodine as the source of iodine atoms, air as the terminal oxidant and sodium nitrite as the catalyst [56]. 1,3-Dipolar cyclo-additions of different hydrophobic nitrones have been studied in both homogenous organic solutions and aqueous suspensions. Here, reactions in water suspensions showed great rate accelerations over homogenous solutions [57]. The rearrangement of benzil is base catalyzed procedure under conventional conditions. In this reaction at high temperatures, water between 300– 380°C (Near critical water) proceeds solely by base catalysis with more environmentally benign medium [58]. A convenient and clean on water mediated synthesis of benzothiazoles/benzothiazolines is reported. Aromatic, heteroaromatic and styryl aldehydes are converted to 2- substituted benzothiazoles in high yields in a one-pot reaction with 2-aminothiophenol in water [59]. Thioesters can be prepared by direct reaction of tertiary thioamides

and alkyl halides in water and in the presence of catalytic amounts of Sodium iodide (NaI), hexadecyltrimethylammonium bromide (HTAB) and 1,4-diazabicyclo[2.2.2]octane (DABCO) [60]. Novel SO<sub>3</sub>H-functionalized ionic liquids bearing two alkyl sulfonic acid groups in the imidazolium cations were designed and successfully applied as catalysts for the one-pot Fischer indole synthesis in water medium [61]. Usually organic solvents are considered to be necessary for the best efficiency in the reactions of aliphatic nitro compounds; it has been shown that these reactions are also very efficient using water as reaction medium [62]. Superheated water has organic solvent like properties and behaves as ideal low cost green solvent for chromatography and other separation methods avoiding use of hazardous solvents [63].

### Conclusion

Green chemistry has come a long way since its birth in 1991, growing from a small grassroots idea into a new approach to scientifically-based environmental protection. All over the world, governments and industries are working with “green” chemists to transform the economy into a sustainable enterprise. Green chemistry includes the technologies of the invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances and where possible utilize renewable raw materials. Replacement by natural or less hazardous reagent to the harmful reagents makes environment pollution free.

In organic synthesis various newly discover solvent and catalyst help to reduce long reaction time. Computer aided designing also provide important tools to reduce reaction time. By the use of appropriating methods and handling of chemicals there is reduced risk of environmental contamination reactions. Implementation of suitable technologies and methods also help to improve the green chemistry some examples are microwave synthetic tools to the preparation of chemical compounds and drugs, computer aided drug design, using green solvents, green catalyst etc.s

### Future directions

Green chemistry may be the next social movement that will set aside all the world's differences and allow for the creation of an environmentally commendable civilization.

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