

A COMPLETE OVERVIEW ON GREEN ANALYTICAL METHOD OF VALIDATION

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ABSTRACT

Although the traditional approach of analytical analysis is excellent and produces very accurate results, there are a number of issues with it. which had the worst impact on analysts and the environment. Instead, the GAC approach should be used to modify the conventional method. That approach ought to be modified in a way that is less damaging and extremely accurate, with minimal environmental impact. GAC, which adheres to the twelve ideals. There are numerous techniques and methods available to create new green conventional methods. A number of metrics tools were available to evaluate the green strategy. That article, which provided everything in a clear and comprehensive manner.

KEYWORDS: Green analytical chemistry, Greenness, Analytical method, Miniatures, Metrics tools.

INTRODUCTION

In our society, the colours that represent various things without telling any word show a lot of things. Just e.g, Green colour represents the environment, eco-friendly, substantial, non-hazardous, and cost-effective. Similarly, in analytical chemistry, the greener version should also be present there. We all know it as 'Green Analytical Chemistry' GAC. The definition of green chemistry was stated by Anastas in 1990.^[1] GAC has been a new emerging chemistry since 2000.^[2]

In analytical work, green chemistry should go beyond the analytical work and be integrated with the environment, education, health, safety, and industry.^[3] Green chemistry technique, which is used to eliminate or reduce the things that cause the worst harm to the environment, human beings, etc.^[4] In green chemistry, the main components are chemicals which was used in different methods, formulations, extractions, and developments. This is a major worsening impact that should be produced. Various organic solvents should cause the greenhouse gas effect. In the industry, various analytical work should be done on multiple kinds of chemicals, and a large amount of waste material is generated in the process, which is toxic and directly impacts nature. The approach of green chemistry in various industries.^[3]

GAC is basically based on 12 principles, which were proposed by Anastas.^[1] Now, which was synonymous with 'PRODUCTIVELY' for the green engineering and for green analytical chemistry, the synonym was 'SIGNIFICANCE'.^[2]

In GAC, the solvent selection is the most important and crucial thing. In analytical chemistry or other departments, a lot of solvents should be used. Most of the organic solvents which was used are hazardous to the analyst and the environment. So the selection of a proper solvent is important to get a robust and rigorous outcome. Tools that have to select a solvent that was present in their.^[5] Ideally, 'no solvent' is better than the use of a solvent, but many more analytical techniques require the use of a solvent.^[6] Research methodology was a systematic outline to gather the precise data required in analytical work. Which was designed to get an accurate and precise outcome, should be obtained for validation. Do the specific objectives behind methodological innovation dictate the metrics and standards by which their performance is subsequently judged.^[1]

The various analytical instrument should be use in industry and laboratory. This should essential to analysis the sample. During the analysis various solvent and gases should us which hazardous and combustible also. In green chemistry in its principles one element is energy.^[1] During process lot of energy which was required so ultimately which was impact on the environment. Some instrument which work on that and reduction of waste.

When large amount solvent required then the generation of wastage also more. So some instrument which require very less amount of sample, solvent and energy. Waste also less generated.

To evaluate the process there was many metric tool are present which was based on the 12 GAC principles. With these tools we know that how our process impact on the green principles. With the references of 12 principles the metric tool which create their criteria on that basis give the score or shows the result with diagrammatic representation. On that give the clarity of the work.

PRINCIPLES OF GAC

Anastas and warner stated that 12 principles on that the GAC stand.^[3] Which was basically based on framework of GAC. 1) life period of chemical in all stage. 2) reduce the hazard of process and chemical final product.^[3] In that the all 12 parameters which was directly associated with environment and health.

- 1) Prevent or minimize the waste.
- 2) Atom Economy is great chose that methodology.
- 3) Select less harmless chemicals.
- 4) Use substance when it need.
- 5) Select that thing which required low amount of energy.
- 6) Choose such product which easily degrade.
- 7) Renewable materials should use.
- 8) Choose the chemical procedure, which minimal impact.
- 9) Minimize the derivatization
- 10) Select appropriate catalyst.
- 11) Safer chemical select.
- 12) Select method which pollution free.

GREEN SOLVENT SELECTION

The million of liters solvent which needs for various process in the world. Which drastically worsen impact produce on environment.^[7] In early decades industry and government which work on that. In pharma industry lot of waste are generated and produced green house gases than automobile industry.^[8] Now various company's which work on that solvent.

In figure 1 shows that which thing is require for the any process in pharmaceutical industry. Massive amount of solvent should require for manufacturing, method validation, and different process should major component which was contribute to harmful and unacceptable effect on environment and analyst.

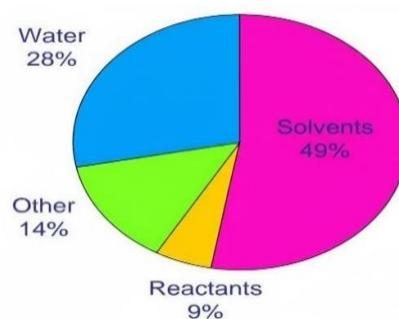


Fig. 1: composition of pmi by acg green chemistry instituted.^[9]

Which work on that to select most appropriate solvent for analytical work which should greener. The guide for solvent selection was their for analytical work. Gsk, pfizer and astrazeneca etc. produced list to which solvent should be used.^[5, 9,10]

Guidelines which provides by companies to the chemist for solvent selection.^[10] Chose right solvent which was green and gave the robust analytical outcome like a original one. Some solvent which categories in that form their greenness.

Pfizer Medicinal Chemistry Solvent Selection Guide		
Preferred	Usable	Undesirable
Water	Cyclohexane	Pentane
Acetone	Heptane	Hexane(s)
Ethanol	Toluene	Di-isopropyl ether
2-Propanol	Methylcyclohexane	Diethyl ether
1-Propanol	Tetrahydrofuran	Dimethylmethane
Ethyl Acetate	Isooctane	Dichloroethane
Isopropyl acetate	Acetonitrile	Chloroform
Methanol	2-MeTHF	NMP
MeOH	Toluene	DCE
1-Butanol	Xylenes	Pyridine
γ -Butanol	DMSO	DMAC
	Acetic Acid	Dioxane
	Ethylene Glycol	Dimethylsulfoxide
		Benzene
		Carbon tetrachloride

Fig. 2: pfizer medicinal chemistry solvent selection.^[9]

In fig 2. Shows that various organic solvent which was categories in 3 section.1 section list of organic solvent which was ideal for the green chemistry which was have very low impact on environment and are less harmless to human. In 2 section list of solvent which was acceptable which show moderate effect on the both environment and health of humans. In 3 section list of chemical which was undesirable which was more harmful and major worsen effect which was produced on the environment which was not acceptable.

SAMPLE PREPARATION TECHNIQUES

Sample preparation which very crucial step for method validation. Lot off solvent should be required for the sample preparation. To dissolve the solute require more amount of solvent. to reduced the amount of solvent there are several methods or techniques was presented.^[4]

1. Microwave-assisted extraction (MAE):- firstly proposed the method in that the microwave energy which was used.^[4] Which required the less amount of solvent than convective method.
2. Supercritical fluid extraction (SFE):- CO₂ Supercritical fluid which was use to reduce the solvent amount. Pressurised fluid extraction (PFE):- it near to similar the soxhlet extraction. Which have extraction efficiency is more required less amount of the solvent.
3. Solid-phase micro extraction(SPME):-use direct sorption of analytes from sample. The extract directly desorbed(all over).
4. Stir-bar sorptive extraction (SBSE):- interaction between analytes and coating material on magnetic rod.
5. Liquid-phase micro extraction (LPME):-it require less amount of solvent for extraction. Which is emerging technique.

MINIATURISATION TECHNIQUE

Miniaturisation is downsizing technique.^[11] for GAC to reduce the sample size, less energy usages, reduce consumption of reagent. To significantly reduced the environmentally. reducing the waste which was generated during the processes. Lower sample size less wastage was generate. Significantly less time require and low amount of energy used.

- Lab-on-chip is effective and capable technique which separate the solvent in 10 second. In that the device consist of column, injector and valves.^[11]
- Capillary electrophoresis require less sample size and buffer system. In that the capillary column was use so, less energy should require.^[11]
- Nano liquid chromatography in that Nano size molecules column was use which ultimately require less amount of sample and less energy require.

CHROMATOGRAPHIC TECHNIQUES

In green analytical technique the various instruments which was used for analysis the sample. Which was all over work on the different principles. UV spectroscopy, HPLC, Gas chromatography, Mass spectroscopy and IR spectroscopy. Electrophoresis technique should also used their.

Liquid chromatography which was widely used technique because determination of large compound and its conventional technique but its produced more amount wastage.^[12] Which was harmful to health and environment. Reducing the solvent consumption and developed

most appropriated technique which reduce or eliminated toxic solvent. For chromatography such points should be considered.

- Selection of stationary phase :- select the stationary phase, which separation time should be less therefore require less amount of mobile phase. Require less time and energy if the diameter of column is small so, the flow rate also less. Similar the stationary phase or material which use for packaging the column which was smaller in size which efficiency of column was increase.
- Selection of mobile phase:- To developed eco-friendly method selection of mobile phase which have less environmental impact. water is ideal solvent which was less toxic and harmless. Mostly acetonitrile which was used as mobile phase because its low viscosity but which was toxic organic solvent which highly impact on both environment and human health.

Methanol also use as solvent which was toxic in nature and ethanol which alternative of methanol which was less harmful than acetonitrile and methanol. Which select the mobile phase in proportion of two or more organic solvent which significantly reduced the time of separation.^[12]

- Secondary equilibrium for sustainable mobile phase:- the addition of secondary substance(chiral reagent, surfactant, cyclohexatriene, ionic agent, etc.) which was secondary substance in between the mobile phase and stationary phase which increase seperability of analytes which reduced the separation time.^[12]

METRICS TOOLS

To judging greenness of analytical method the metrics tools which was developed according to the GAC principle.^[1] Based on the 12 GAC principles the various metric tools which was developed.^[12,13,14] the first approach was NEMI later on ECO-SCALE, AGREE, GAPI, AMGS, MCDA, HEXAGAON, 12RGB, BAGI.^[12,15,16,17,18,19] evaluation is crucial step in analytical method development to known the impact of that method which was produced and which helpful for selecting the most appropriated method which was less impact on environment and human health.

1. NEMI:- It is a first metric tool which was developed MDCB.^[20] National environmental method index (NEMI) represented as in form of pictogram their was four field represent the different aspect.^[18, 19] The respective field shows green colour means the respective have not hazardous and friendly.

Is very conventional to read the pictogram. First field of pictogram are non coloured represent as the analytical procedure which present on the persistent, bio-accumulative, and toxic list.^[20] Second field represent green means non of solvent use which was the hazardous so less hazardous waste was generated.^[14] Third part shows green coloured means pH of sample is range in 2 to 12Click or tap here to enter text. mean its non corrosive.^[18,19] Fourth part green coloured means the waste generation which was less than the 50 gm.

Advantages

- Easy to read, simple.
- About environment and procedure information in the pictogram.

Disadvantage

- Not quantitative and qualitative estimation..
- Not clear idea about chemical consumption and energy.
- Not give the value.

2. ECO-SCALE:- the system which was have a total 100 penalty point to get 100 point represent ideal green analysis.^[18,19] GAC tool which developed in 2012(1). Point was dedicated on amounts off energy, solvent consumption, waste generation on that point was minus.^[21] It is semi quantitative technique.^[12] Green is the technique for 75+ and 50-75. Poor green analysis is under 50. Non-toxic substances are neither penalized or marked with symbols.

Use of solvent less the 10ml or gm get 1 point. Between 10 to 100 ml or gm get 2 point. More than that get 3 penalty point.^[12] The energy consumption is less than 0.1 Kwh get 0 point. Between 0.1 to 1.5 Kwh get 1 point and more than that get 2 penalty point. waste generation is less than the 1 g or ml get 1 minus point. In between 1 to 10 g or ml get 3 point and more than that get 5 penalty point.^[20] Similar like that the all aspect was check.

Advantage

- Provide quantitative information.
- Simple to understand.

Disadvantage

- Lack of environment information.
- Give a number without information.

3. AGREE:- This software AGREE is a simple and all-inclusive instrument for evaluating the environmental friendliness of analytical tests, yielding results that are clear and easy to understand. The 12 GAC principles are converted into a 0-1 scale and used to calculate the AGREE metric. Additionally, the evaluation of these 12 GAC principles determines the ultimate score of this GAC metric.^[19]

The objective of AGREEprep is to fill this gap by providing a thorough GAC metric grounded in the 10 GSP principles. The GSP guidelines state that AGREEprep carefully assesses how environmentally friendly sample preparation methods are.^[20] The pictogram's centre area has 10 elements that correspond to the ten GSP principles.^[17] In the AGREEprep picture, each segment's colour can change from dark green (score of 1) to red (score of 0).^[19]

Advantages

- It cover 12 GAC principle.
- It coloured based approaches.

Disadvantages

- Not consider energy, chemical and waste.

4. GAPI:- The GAPI pictogram's five pentagrams can be used to assess and determine how green certain phases of the entire analytical process are to show the greenness of various phases of the full analytical process, a three-level colour scale is used in the GAPI pictogram. Green, yellow, and red colours, respectively, indicate low, medium, and high impact of the analytical method on the environment and human health.^[20]

- First pentagram is for sampling have 4 field.
- Second pentagram is for type of method.
- Third pentagram is for step preparation for sample.
- Fourth pentagram is for amount off solvent.
- Fifth pentagram is for energy consumption.^[19]

The idea behind the tool's creation was to enable it to evaluate as much data as possible regarding a particular analytical approach, including steps taken before analysis, in order to provide a more thorough assessment of the procedure's "greenness." We think that this tool satisfies these requirements. A tool called the Complex Green Analytical Procedure Index

(ComplexGAPI) addresses every facet of an analytical process, from sample preparation and final analysis to sample collection, transportation, preservation, and storage.^[18]

Advantage

- It is simple method.
- It cover all step from sample to final step.

Disadvantage

- Not cover synthesis part.
- Not get information about hazard.

5. AMGS:- Analytical method greenness score is analytical method that is semi-quantitative Greenness Score is used to assess the environmental impact of analytical procedures. Solvent safety is affected by a number of factors, including the geometric mean-based SHE computation.^[19] The sustainability of a method shouldn't be determined by scores. Eco friendliness is decreased by AMGS scores. AMGS research Effects of the approach on solvent health, safety, and the environment. AMGS puts safety, instruments, and solvents first.

We integrated the AMVI for method solvent consumption with extra solvent SHE variables from the solvent selection guide (SSG), which includes the total in Green Chemistry Accepted Manuscript usage CED, to produce a more thorough method assessment tool. In contrast to earlier green calculators, this next-generation tool measures the greenness of particular analytical or preparative procedures by taking into account instrument energy usage in addition to the SSG values from the earlier solvent energy guides. A weighted combination of three characteristics is used to determine the AMGS: CED for the solvent and instrument, SHE/SSG factors for solvent safety, and AMVI for solvent volume waste.^[19]

Advantages

- Highlight environment, safety, life cycle concern.
- Easy to understand.

Disadvantage

- User need baseline knowledge of analytical work .
- Not capture fully metric for hazard.

6. HEXAGON:- In the hexagon quantitative tool, five variables of a method are rated by allocating penalty points (PPs). Environmental friendliness, sustainability, economic cost, linked chemical and health concerns, and analytical traits or figures of merit are the five categories into which the variables are separated. The analytical performance of the approach being evaluated is specifically included in the figures of merit, which are arranged into various blocks.^[16]

The carbon footprint metrics quantify the environmental impact by taking into account the time required to complete the analysis as well as the energy consumption of the equipment used. The associated yearly cost of the analytical determination is calculated using the salary paid to skilled persons, the cost of the reagents and materials utilized, and the cost of the equipment required in addition to its electricity consumption cost.^[16]

Last but not least, a hexagon-shaped pictogram is created by organizing the total of the PPs, estimated carbon footprint, and cost values on a 0–4 scale for each variable. The greater the score (i.e., approaching 4). The scale corresponds to the following scores: 0, 1, 2, 3, and 4, which represent excellent, good, appropriate, weak, and fail performance of the examined analytical procedure. Numerous approaches that make use of various analytical techniques have implemented the hexagon algorithm.

Advantages

- Provides compressive information of all aspects of GAC.
- Result are easy to interpret.

Disadvantages

- Calculation process are complex.
- Require complete and compressive detail so it is a time consuming process.

FUTURE PROSPECTIVE AND CHALLENGES

Future Prospective

To developed new eco-friendly method which have less impact on environment and health. There is still a lot of potential for Green Analytical Chemistry (GAC) to influence future sustainable research, business operations, and laws. The scope of GAC is anticipated to grow in a number of ways as a result of increased environmental consciousness and more stringent sustainability goals in the chemical and pharmaceutical industries.

- Regulatory Framework Integration Sustainability:- In analytical processes is important to international regulatory agencies like the FDA, EMA, and CDSCO. Analytical technique validation in the future can call for proof of environmental compatibility backed by GAC metrics in addition to quality and repeatability.
- Progress in Eco-Friendly Solvents:- One of the main priorities is still the development of renewable, biodegradable, and non-toxic solvents. Research on bio-derived solvents, supercritical fluids, deep eutectic solvents, and ionic liquids could transform sample preparation.
- Miniaturization and Automation:- with the help of Ai miniaturization automation we reduce the consumption of solvent consumption so reduce the energy and waste generation.
- Renewable energy:- instruments require the lot of energy. At laboratory level shifting toward to sustainable energy.
- Metrics :-many advanced tools which was available with the help of AiML to make more effective tool and accelerated the scoring method.

Challenges

- Balancing greenness and analytical performance is major challenge greener solvent miniaturization which hamper the sensitivity.
- Limitation of greener solvent is major concern.
- High cost of green technology so it is not possible at small laboratories level.
- Complex to hand on the metric tools its have very complex algorithm.
- Waste management is concern that too manage the generated waste in proper way.

CONCLUSION

This study give the complete overview on the GAC. Which promote the green chemistry to show the sustainability and eco friendliness to environment. Without the hampering the accuracy. selection of solvent and their criteria without compromising. Miniaturising technique which reduces the solvent consumption. metrics tools which was to assessed the process. Time to move forward than conventional method. Challenge is to adoption the technique at industry level and it is cost which have high at starting point so difficult at small level. The study scope to create safe, efficient and eco-friendly and met the regulatory compliance.

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