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A COMPUTATIONAL FRAMEWORK FOR MODERN HERBAL DRUG DEVELOPMENT: "GREEN EXTRACTION AND EFFECTIVE GREENNESS METRICS"

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ABSTRACT
Growing awareness of environmental sustainability has driven considerable interest in developing analytical extraction practices that align with green chemistry ideals. Traditional approaches to isolating plant-derived bioactive compounds rely on large volumes of toxic organic solvents, energy-intensive operations, and prolonged processing times, all of which contribute to safety hazards and environmental burden. In response, green extraction methodologies have emerged as viable alternatives that prioritize reduced solvent toxicity, lower energy demands, and maintained or improved extraction performance. This article presents a comprehensive overview of recent advances in green extraction science as applied to phytochemical research, with particular attention to techniques such as ultrasound-assisted extraction, microwave-assisted extraction, and supercritical fluid extraction. In addition, this review discusses the growing importance of greenness assessment tools as quantitative frameworks for evaluating the environmental sustainability of extraction procedures. Metrics that account for solvent consumption, energy usage, waste output, and overall process efficiency are systematically examined. The synergistic application of green extraction approaches alongside computerized greenness evaluation platforms provides a unified, evidence-based strategy for selecting the most environmentally responsible extraction methods. Collectively, these developments support the broader transition toward greener and more efficient research practices in phytochemistry and related scientific disciplines.

KEYWORDS: Green extraction, Phytochemicals, Coventional, Green chemistry, Eco friendly, Greenness, Environmental sustainability, Greenness metrics, Green solvents.

INTRODUCTION
Extraction constitutes a foundational step in the recovery of biologically active constituents from botanical materials, serving as the initial process through which secondary metabolites are isolated from plant matrices ***(Dhanani et al., 2015).*** The quality and composition of the resulting extract are critically determined by the extraction strategy employed, making method selection a pivotal decision in phytochemical research.

Historically, medicinal plant extractions have been conducted using established conventional techniques including Soxhlet extraction, hydrodistillation, steam and water distillation, maceration, cohobation, enfleurage, and heating reflux methods. These approaches have found widespread application in the food, fragrance, and pharmaceutical industries. However, they share several critical shortcomings: These methods present several well-documented limitations from both operational and environmental standpoints. Processing durations are typically prolonged, resource demands are considerable, and the selectivity of extraction is often poor. Residual solvent contamination in the final product remains a persistent concern, as does the susceptibility of thermolabile phytoconstituents to structural degradation under high-temperature conditions. The pharmacological activity of target compounds may also be compromised during processing, and the downstream disposal of hazardous solvent waste poses an ongoing environmental challenge ***(Majid et al., 2023)***. These limitations have stimulated the search for newer, more sustainable extraction approaches.

The role of plant-based extraction spans centuries of human history, from the ancient crafting of perfumes and herbal remedies to contemporary pharmaceutical and food manufacturing. Despite this long tradition, conventional techniques remain dependent on hazardous solvents and energy-intensive workflows, which are increasingly incompatible with modern sustainability goals. This tension between established practice and environmental responsibility has catalyzed a paradigm shift toward greener extraction approaches ***(Kirusnaruban et al., 2025)***.

Green extraction methodologies were developed specifically to address the environmental and safety drawbacks associated with conventional processing. By employing environmentally benign solvents such as water, bioethanol, biomethanol, ethyl acetate, and ethyl lactate, these methods achieve significant reductions in environmental impact ***(Martins et al., 2023).*** Modern green techniques such as ultrasound-assisted solvent extraction (UASE) and microwave-assisted solvent extraction (MASE) are increasingly employed alongside conventional methods like maceration and Soxhlet extraction. The selection of the most appropriate method is important because extraction technique directly influences the biological activity profile of the resulting extract and its pharmacotherapeutic utility ***(Dhanani et al., 2015)***.

Non-conventional extraction techniques are inherently non-thermal and environmentally compliant in nature, conforming to the guidelines of the Environmental Protection Agency. These approaches require lower solvent volumes, operate with reduced energy consumption, offer shorter extraction durations, and produce higher yields compared to classical methods ***(Dhanani et al., 2015)***. The concept underpinning green extraction is rooted in the e3 principle, which aligns with the United Nations 2030 sustainable development strategy and encompasses six key aspects: well-defined sourcing, limitation of organic solvent use, minimization of energy consumption, avoidance of by-product generation, reduction of extraction duration, and recovery of natural ingredients ***(Majid et al., 2023)***.

The application of greenness metrics provides a systematic and quantitative framework for evaluating the environmental performance of analytical procedures, enabling researchers to make informed comparisons and select the most sustainable methods for their specific applications.

Definition of Green Extraction

At its core, green chemistry represents a scientific philosophy oriented toward the proactive prevention of chemical hazards — prioritizing the design of processes and products that inherently avoid the formation or deployment of toxic substances, rather than addressing their consequences after the fact. When this philosophy is extended to the isolation of phytochemicals, it forms the conceptual basis of green extraction — a field committed to developing resource-efficient, ecologically responsible methods for recovering bioactive constituents from plant matrices***(Chemat et al., 2012).***

In practical terms, green extraction encompasses processes designed to achieve the following objectives ***(Chemat et al., 2012)***

- Reduction of overall energy consumption
- Utilization of alternative solvents such as supercritical CO2, water, or ethanol
- Incorporation of renewable biological materials
- Conversion of extraction by-products into useful co-products
- Production of high-purity, high-quality, and safe extracts

Green extraction therefore refers to environmentally conscious methodologies applied to obtain valuable phytochemicals such as bioactive molecules, oils, pigments, and flavors from natural sources, with plants representing the most commonly exploited substrate.

Solvents Employed in Green Extraction: Green Solvents

Solvents occupy a central position in the extraction process, fulfilling roles in solution preparation, phytoconstituent enrichment, solvent exchange, sample preservation, dilution, analytical separation, and surface cleaning. A well-chosen solvent must exhibit appropriate extraction capacity while preserving the structural integrity of the target molecules throughout the process.

For a solvent to qualify as green in the context of phytochemical extraction, it must satisfy a constellation of environmental and safety criteria. These include a minimal tendency toward atmospheric evaporation, low combustibility, an absence of respiratory or systemic toxicity, and freedom from carcinogenic potential. Beyond acute safety concerns, genuine green solvents must also be amenable to recovery and reuse following extraction, and must break down readily in biological or environmental systems without accumulating as persistent pollutants***(Martins et al., 2023)***. These properties collectively minimize the ecological and health risks associated with solvent use.

Commonly employed green solvents include.

- Water
- Supercritical carbon dioxide
- Deep eutectic solvents
- Ionic liquids

- Biosolvents, including esters derived from natural organic acids (ethyl acetate, ethyl lactate), fatty acid esters, bioalcohols (bioethanol, biomethanol), terpene compounds (eucalyptol, limonene), isosorbide, and glycerol derivatives

Significance of Green Extraction in Contemporary Research

Environmental sustainability has become a priority concern across all countries, and the scientific community has recognized that continued progress in herbal extraction is feasible only when research practices align with ecological preservation goals, particularly with respect to reducing carbon footprint. Conventional extraction techniques such as maceration and percolation demand substantial quantities of organic solvents and tend to be time-consuming while delivering lower yields. In contrast, modern alternatives — including Microwave-Assisted Extraction (MAE), Ultrasound-Assisted Extraction (UAE), Pressurized Liquid Extraction (PLE), Supercritical Fluid Extraction (SFE), and Enzyme-Assisted Extraction (EAE) — have demonstrated superior energy efficiency and enhanced phytoconstituent recovery compared to their classical counterparts.

Green extraction minimizes solvent waste generation and reduces health and occupational risks. The scale of solvent dependency in pharmaceutical production is substantial — published estimates indicate that solvent disposal constitutes the dominant fraction of total process waste generated during API manufacture, often representing upwards of four-fifths of all waste streams, which reinforces the urgency of transitioning toward greener solvent strategies ***(Raj et al., 2022).*** Natural extracts obtained through green methods retain a full complement of phytoconstituents including proteins, lipids, dietary fibers, carbohydrates, antioxidants, essential oils, and fragrances, all of which can be sourced from diverse plant materials.

Representative examples of green extraction techniques and their documented applications include.

1. Ultrasound-Assisted Extraction (UAE) — Applied to the extraction of catechins and polyphenols from Camellia sinensis
2. Microwave-Assisted Extraction (MAE) — Used for the recovery of polysaccharides and phenolic compounds from Aloe vera
3. Supercritical Fluid Extraction (SFE) — Employed for ginsenoside isolation from Panax ginseng
4. Pressurized Liquid Extraction (PLE) — Utilized in flavonoid extraction from Ginkgo biloba
5. Enzyme-Assisted Extraction (EAE) — Applied to resveratrol recovery from Vitis vinifera
6. Deep Eutectic Solvent Extraction (DES) — Used for glycyrrhizin isolation from Glycyrrhiza glabra
7. Pulsed Electric Field Extraction (PEF) — Applied to pigment and antioxidant recovery from Spinacia oleracea

Foundational Principles of Green Extraction *(Chemat et al., 2012)*

The six principles of green extraction of natural products serve as a guiding framework for both industry practitioners and academic researchers. They are intended to define an innovative, environmentally certified standard that encourages systemic improvement across all aspects of solid-liquid extraction processes.

1. **Principle 1:** Innovation through the selection of diverse plant varieties and the utilization of renewable plant resources.
2. **Principle 2:** Preference for alternative solvents, principally water and agro-derived solvents.
3. **Principle 3:** Reduction of energy consumption through heat recovery and the adoption of innovative technologies.
4. **Principle 4:** Generation of valuable co-products rather than waste, supporting bio- and agro-refining industries.
5. **Principle 5:** Reduction of the number of unit operations, with preference for safe, robust, and controlled processes.
6. **Principle 6:** Production of extracts that are non-denatured and biodegradable, free from chemical contaminants.

Tools and software used to evaluate green extraction

1. Green Extraction Tree (GET)
2. Path2Green
3. Analytical GREEnness Metric and Software (AGREE)
4. Analytical GREEness Metric for sample preperation (AGREEprep)
5. Green Analytical Procedure Index (GAPI)
6. Complex Green Analytical Procedure (ComplexGAPI)
7. Modified Green Analytical Procedure Index (MoGAPI)
8. Complex Modified Green Analytical Procedure Index **(ComplexMoGAPI)**

1) GREEN EXTRACTION TREE (GET)

✓ A Novel Tool to Greenness Metric for Green Extraction of Natural Products

The Green Extraction Tree (GET) is an intuitive and comprehensive evaluation tool developed specifically to quantify the environmental sustainability of sample preparation in natural product extraction. Its assessment framework integrates the ten principles of green sample preparation with the six principles of green extraction of natural products, thereby covering the entire extraction workflow encompassing samples, solvents and reagents, energy consumption, by-products and waste generation, process risk assessment, and extract quality. The GET visually represents results using a tree-shaped pictogram with six branches, where color-coded leaves — green, yellow, and red — correspond to low, moderate, and high environmental impact respectively. Numerically, these categories are assigned scores of 2, 1, and 0, which collectively allow for horizontal comparisons of the greenness of different extraction procedures ***(Fan et al., 2025)***.

The GET was developed on the conceptual foundation of Green Extraction of Natural Products (GENP) as originally proposed by *Chemat* in 2012. Recognizing the absence of appraisal tools specifically designed for natural product green extraction, the GET was constructed by integrating both the ten principles of green sample preparation (GSP) and the six principles of GENP, resulting in a unified tool comprising 14 evaluation criteria distributed across six thematic branches: sample characteristics, solvents and reagents, energy consumption, by-products and waste, process risk, and extract quality. The tool evaluates factors such as the use of vulnerable or endangered raw materials, industrial scalability, energy consumption (kWh per sample), and solvent toxicity using standardized NFPA hazard ratings. GET also serves as an accessible educational resource for students and researchers seeking to understand and apply green extraction principles ***(Fan et al., 2025).***

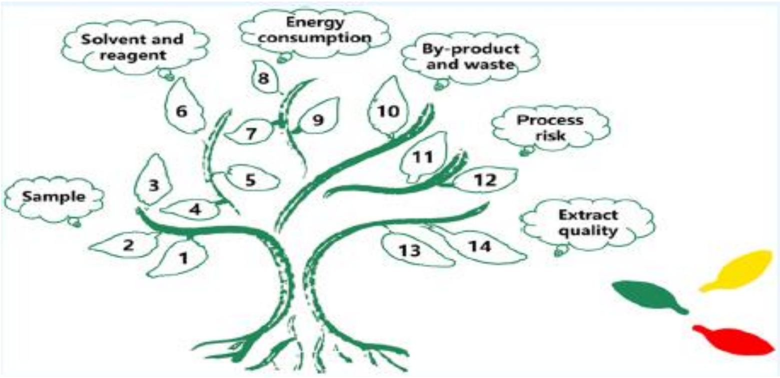

Figure 1: Green Extraction Tree pictogram with description*(Fan, L. et al., 2025)*.

Scoring and interpretation

□ Color Coding:

□ Green = low environmental impact

□ Yellow = moderate environmental impact

□ Red = high environmental impact

□ Points:

Green = 2

Yellow = 1

Red = 0

Table 1: Metric Criteria of Green Extraction Tree (GET) tool:*(Fan, L. et al., 2025)*.

Category	Criterion	Green	Yellow	Red
Samples	Promote the use of renewable materials (1)	Sustainable or renewable raw materials and extraction solvents	With 50% or more of materials and solvents as sustainable or renewable resources	With less than 50% of the materials and solvents as sustainable or renewable resources
	Ensure sample stability and simplify sample storage (2)	Under normal conditions	Under appropriate physical or chemical conditions	Under appropriate physical and chemical conditions
	Minimize sample amounts (3)	<0.1g	0.1-1g	>1g
Solvent and reagents	Use safer solvents and reagents (4)	Green solvents and other safety reagents used	Green solvents and other petrochemical solvents used	Only petrochemical solvents used
	Minimize solvent and reagent amounts (5)	<10 mL (<10 g)	10-100 mL (10-100 g)	>100 mL (>100 g)
	Minimize additional sample preparation steps (6)	No additional operations beyond the extraction step	Simple treatments (liquid-liquid extraction, enrichment, etc.)	Advanced treatments (derivatization, hydrolysis, etc.)
Energy consumption	Minimize energy consumption (7)	<0.1 kWh per sample	0.1-1 kWh per sample	>1 kWh per sample
	Maximize sample throughput (8)	>10 samples h^{-1}	5-10 samples h^{-1}	<5 samples h^{-1}
	Maximize the extraction efficiency of target compounds (9)	Compared with existing methods increase by more than 10%	Compared with existing methods increase by 5-10%	Compared with existing methods increase less than 5% or no comparative data
By-product and waste	Minimize by-product and waste generation (10)	<1 mL (1g) per gram sample	1-10 mL (1-10 g) per gram sample	>10 mL (>10 g) per gram sample
Process risk	Reduce the risk of health hazards (11)	Slightly toxic, slightly irritant; NFPA health hazard score = 0 or 1	Moderately toxic; could cause temporary incapacitation; NFPA health hazard score = 2 or 3	Serious injury on short-term exposure; known or suspected small animal carcinogen; NFPA health hazard score = 4
	Reduce operational safety risks (12)	No special hazards; NFPA flammability or instability score = 0 or 1	A special hazard is used; NFPA flammability or instability score = 2 or 3	NFPA flammability or instability score = 4
Extract quality	Choose greener analytical detection techniques (13)	Simple, low-energy analytical devices (smart phones, spectrometers, etc.)	Commonly used chromatographic analysis, electrophoresis technology (gas chromatography, liquid chromatography, capillary electrophoresis technology, etc.)	Complex, advanced, high-energy analytical equipment (high-energy gas/liquid phase mass spectrometry, inductively coupled plasma mass spectrometry with high inert gas consumption, etc.)
	Ensure the industrial production prospects (14)	Used in industrial production successfully	With potential for industrial production	Laboratory scale research capability only

2) Path2Green

Path2Green is a decision-support evaluation tool that incorporates twelve principles of green extraction and introduces a novel sustainability metric designed for comparative assessment of extraction pathways. It serves as a guide to direct researchers toward greener extraction choices ***(de Souza Mesquita et al., 2024).*** Unlike conventional single-domain metrics, Path2Green evaluates biomass extraction processes across environmental, social, and economic dimensions, generating a composite score ranging from -1.0 to +1.0, where higher scores indicate superior sustainability performance.

Path2Green provides a nuanced understanding of the environmental consequences of extraction activities from the point of biomass collection or production through to the end of the process. By incorporating parameters such as resource depletion, energy consumption, waste generation, and biodiversity preservation, Path2Green aspires to deliver a holistic assessment of the overall sustainability of an extraction approach. The tool's practical significance lies in its capacity to consolidate complex environmental datasets into a simple, accessible numerical output that facilitates evidence-based decision-making across industrial and academic contexts. Its clear benchmarks and standards incentivize ongoing improvement in sustainability practices ***(de Souza Mesquita et al., 2024).***

The 12 Principles Evaluated by Path2Green

- **Biomass:** Preference for naturally sourced biomass requiring minimal resource usage
- **Transport:** Maintaining biomass integrity while limiting transport-associated environmental footprint
- **Pre-treatment:** Optimization strategies to minimize or avoid pre-treatment steps
- **Solvents:** Minimizing solvent quantities, with priority given to biologically derived, biodegradable, and non-toxic options
- **Scaling:** Ensuring reproducibility and supporting continuous extraction workflows
- **Purification:** Tailoring purification extent to the intended final application
- **Yield:** Maximizing utilization and valorization of the biomass
- **Post-treatment:** Functionalization of natural products after extraction to enhance value
- **Energy:** Prioritizing clean energy sources and high-efficiency extraction equipment
- **Application:** Ensuring safety of the extracted product across multiple application domains
- **Repurposing:** Designing closed-loop extraction systems, preferably using non-virgin materials
- **Waste Management:** Implementing rigorous waste minimization and effective disposal strategies

Validation of the Path2Green metric

Validation of the Path2Green metric was conducted by applying it to published studies on bioactive compound extraction from biomass. ***(de Souza Mesquita, L. M. et al., 2024).***

Advantages of Path2Green tool over other available tools

In terms of advantages, Path2Green functions similarly to a SWOT analysis, enabling researchers to identify weaknesses and areas for improvement within their extraction strategies, thereby supporting the development of greener practices ***(de Souza Mesquita et al., 2024).*** A companion mobile application was developed to streamline scoring and visualization, providing pictographic outputs and a weighted composite score based on environmental, social, and economic contributions

Path2Green Access

- A mobile app was develope**d** specifically to streamline scoring and visualization for the Path2Green metric (e.g., pictograms). It is mentioned in the article that:
- A mobile app exists for inputting scores and generating pictograms.
- The app is available in the *Electronic Supplementary Information (ESI)* of the article.
- It may be downloadable alongside the supplementary files, such as a ZIP or PDF, linked on the journal page.
- Input scores for each of the 12 principles (–1 to +1)
- The app calculates a weighted average based on Environmental, Social, and Economic contributions.
- It outputs a pictogram and final Path2Green score (from –1 to +1).

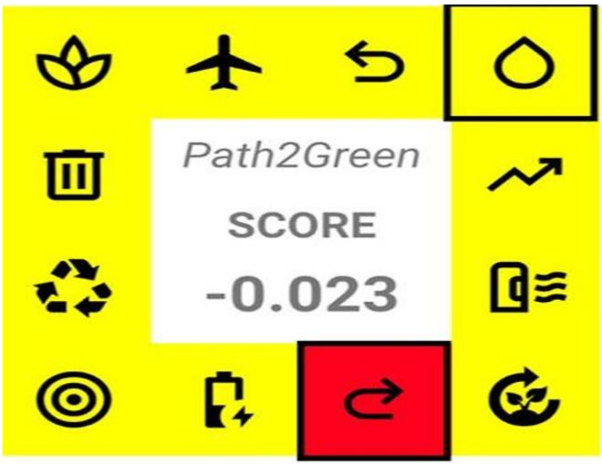

Figure 2: Pictogram depicting the final score of the Path2Green metric (de Souza Mesquita, L. M. et al., 2024).

3) AGREE (Analytical GREEnness metric and software)

The Analytical GREEnness (AGREE) tool was developed by Gdask University of Technology, Poland***(Pepakayala, S. et al., 2025).***

It evaluates analytical methods against the twelve principles of Green Analytical Chemistry (GAC), generating a final score through twelve weighted input variables normalized to a common scale between 0 and 1. The output takes the form of a clock-shaped pictogram in which each of the twelve principles is represented by a colored segment. The color of the central area transitions from red to green as the overall score improves, with scores above 0.6 indicating that the method satisfies green criteria ***(Mahdavi, R. et al., 2024).***

12 principles of Green Analytical Chemistry (GAC) converted by "AGREE" in to a numerical score

- Principle 1: Direct Analytical Techniques Should Be Applied to Avoid Sample Treatment
- Principle 2: Minimal Sample Size and Minimal Number of Samples Are Goals
- Principle 3: In Situ Measurements Should Be Performed
- Principle 4: Integration of Analytical Processes and Operations Saves Energy and Reduces the Use of Reagents
- Principle 5: Automated and Miniaturized Methods Should Be Selected
- Principle 6: Derivatization Should Be Avoided
- Principle 7: Generation of a Large Volume of Analytical Waste Should Be Avoided and Proper Management of Analytical Waste Should Be Provided
- Principle 8: Multianalyte or Multiparameter Methods Are Preferred versus Methods Using One Analyte at a Time
- Principle 9: The Use of Energy Should Be Minimized
- Principle 10: Reagents Obtained from Renewable Source Should Be Preferred
- Principle 11: Toxic Reagents Should Be Eliminated or Replace
- Principle 12: The Safety of the Operator Should Be Increased***(Pena-Pereira, F. et al., 2020).***

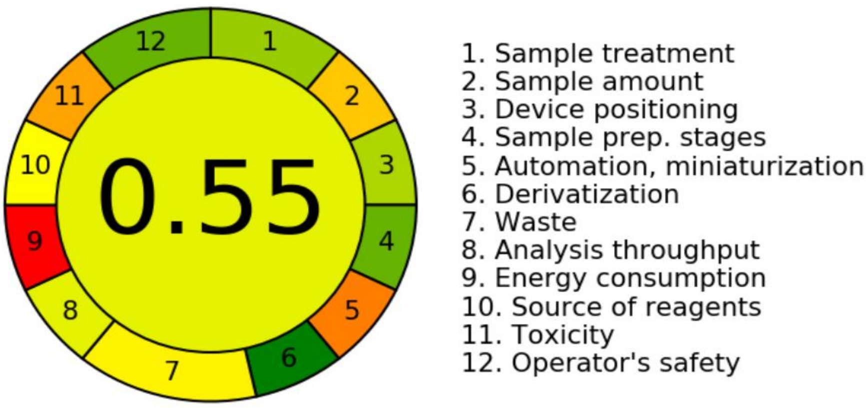

Figure 3: Pictogram of AGREE *(Mahdavi, R. et al., 2024).*

Formula to calculate the overall AGREE score

Final score ranges from **0 (not green)** to **1 (fully green)**

$$AGREE\ Score = \frac{\sum^{12} w_i \times S_i}{\sum_{i=1}^{12} w_i}$$

where:

- S_i = score for the i^{th} principle of Green Analytical Chemistry (0 to 1)
- w_i = weight for the i^{th} principle
- 12 = number of principles

(If all weights are equal:)

$$AGREE\ Score = \frac{S_1 + S_2 + S_3 + \cdots + S_{112}}{12}$$

INSTALLATION---SOFTWARE LINK TO ACCESS "AGREE" TOOL

Evaluation with this tool can be obtained from***(Pena-Pereira, F. et al., 2020).***

The most recent version of the Python code can be obtained from the repository maintained at git.pg.ed.pl/p174235/AGREE

A compiled version is currently available for the Windows operating system and can be obtained from https://mostwiedzy.pl/AGREE

STEPS TO ACCESS THE "AGREE" SOFTWARE: mostwiedzy.pl/AGREE

- ➢ Open the web browser (Chrome, Firefox, Edge, Safari)
- ➢ Type or paste the link "mostwiedzy.pl/AGREE" (official page where the AGREE software is freely available to download) in the address bar.
- ➢ Download or open the AGREE tool

On the AGREE page find the download link to for the AGREE software package

Download the file link to your computer

- ➢ Install or launch the tool
- ➢ Just open the web link (agree-index.anvil.app) provided in the AGREE page
- ➢ Prepare the analytical method data

Before using AGREE collect details regarding the analytical procedure you want to access

- Sample preparation steps
- Solvent and reagent types and amounts
- Waste generated
- Energy consumption
- Automation, throughput, and safety considerations

These data will be input into AGREE according to the 12 principles of Green Analytical Chemistry.

- ➢ Input data into AGREE

Enter values for each of the 12 green criteria

Assign weights to the principles depending on their importance

- ➢ Generate the greenness report

Click "Calculate" or "Generate AGREE"

The tool will produce

- A numerical greenness score between 0 to 1
- A visual interpretation of heavy environmental impact(red) to better(green)
- ➢ Review and export results

Study the output pictogram and score to see which aspects of your method are greener vs less green

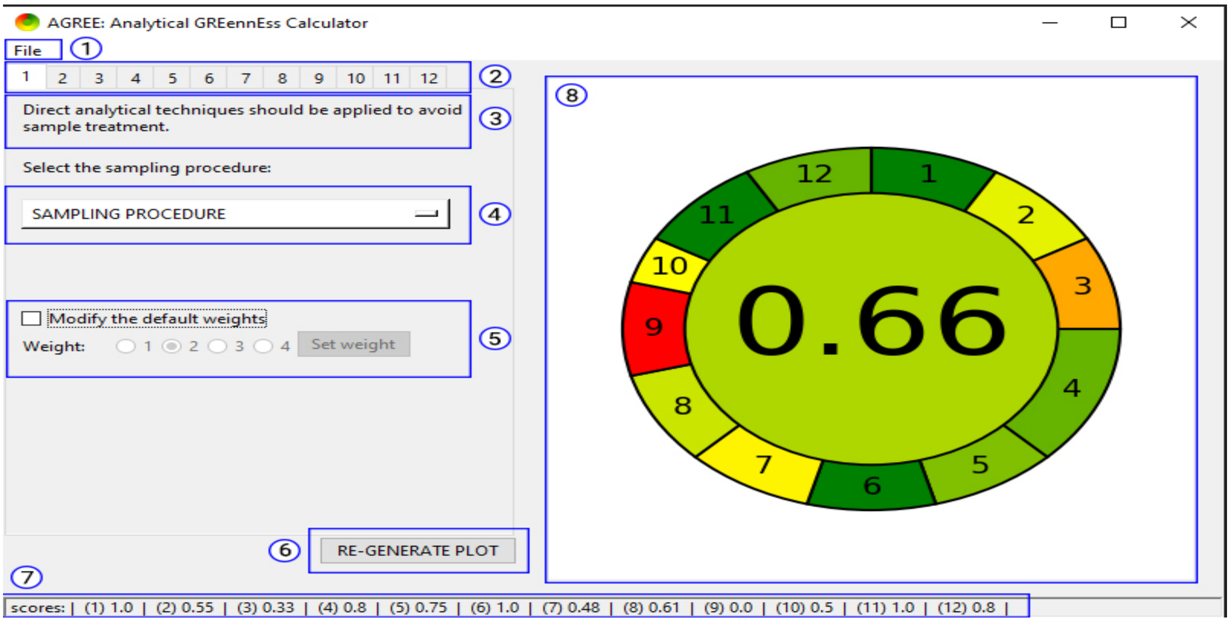

Figure 4: AGREE Circular Visualization of Analytical Greenness Score.

$$\text{AGREE score} = \frac{\sum_{i=1}^{12} F_i}{12} = 1.0+0.55+0.33+0.8+0.75+1.0+0.48+0.61+0.0+0.5+1.0+0.8/12$$

= 7.82/12 = 0.65166 = 0.66

Advantages of "AGREE" over other tools:*(Pena-Pereira, F. et al., 2020).*

It is

- ✓ Comprehensive (by incorporation of each of the 12 principles)
- ✓ Flexible (by the possibility to assign weights)
- ✓ Easy to interpret (the output is a colored pictogram, showing the structure of weak and strong points)
- ✓ Easy to perform (with a user-friendly GUI software)
- ✓ Freely downloadable software makes the analysis very fast and straightforward
- ✓ The analysis can be performed in a few minutes

3) AGREEprep(*Analytical GREEnness metric for sample preparation)*

AGREEprep was developed by *Wojnowski* in 2022 as a specialized greenness assessment tool dedicated exclusively to evaluating the sample preparation step in analytical workflows. It is grounded in ten principles of green sample preparation: (1) favoring in situ sample preparation; (2) using safer solvents and reagents; (3) targeting sustainable, reusable, and renewable materials; (4) minimizing waste; (5) reducing sample, chemical, and material amounts; (6) maximizing sample throughput; (7) integrating steps and promoting automation; (8) minimizing energy consumption; (9) selecting the most environmentally favorable post-sample preparation configuration for analysis; and (10) ensuring operator safety ***(Armenta, S., et al., 2019)***

INSTALLATION---SOFTWARE LINK TO ACCESS "AGREE" TOOL(*Wojnowski, W. et al., 2022)*

The AGREEprep open access software can be obtained from mostwiedzy.pl/AGREEprep, and the code is available at git.pg.edu.pl/p174235/agreeprep

The AGREEprep software generates a round pictogram with a central circle displaying the overall score and ten trapezoidal bars whose lengths are proportional to the assigned weights for each criterion. Scores are expressed on a 0 to 1 scale using the same color coding as AGREE — red (0), yellow (0.5), and green (1) ***(Pena-Pereira, F. et al., 2022).***

AGREEprep can be accessed by following the same steps to access the AGREE software.

Advantages of AGREEprep

Its main advantages include dedicated evaluation of unconventional sample preparation procedures and the ability to assign individualized parameter weights ***(*Kaya, S. I. et al., 2024).**

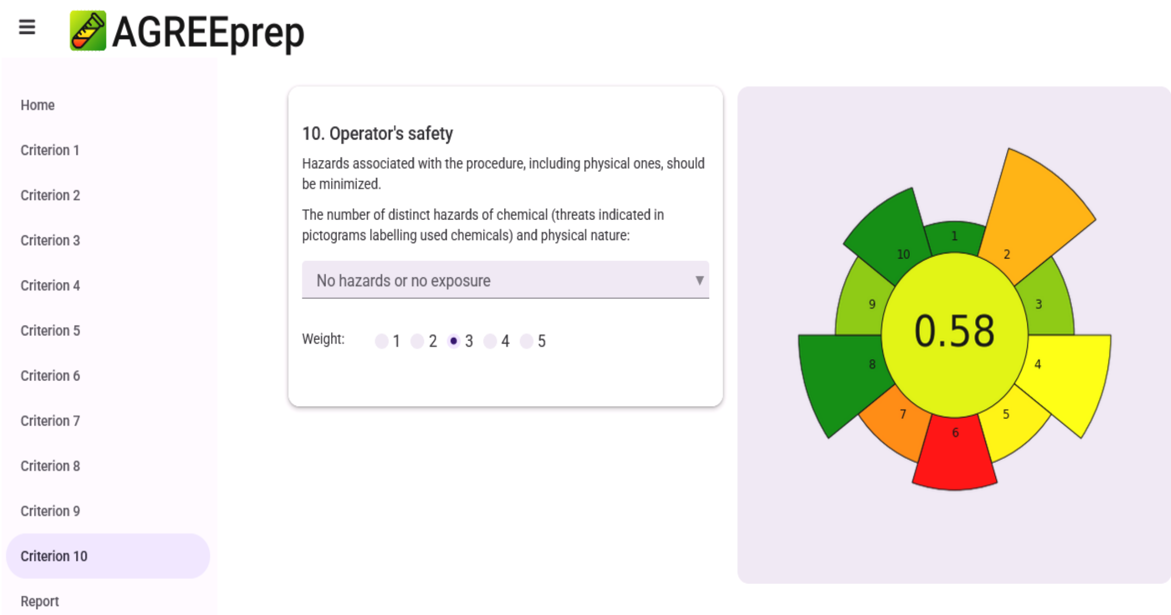

Figure 5: AGREEprep visualization of greeness score.

4) GAPI (Green Analytical Procedure Index)

The Green Analytical Procedure Index (GAPI) is an assessment tool designed to evaluate the environmental impact of analytical procedures used in laboratory settings. Originally proposed by Plotka-Wasylka in 2018, GAPI provides a visual and comprehensive summary of the overall greenness of an analytical method, covering the complete analytical workflow from sample collection to final determination(***Płotka-Wasylka, J. et al., 2018).***

In GAPI, a distinctive symbol composed of five connected pentagrams is used to evaluate and quantify the environmental contribution of each step in the analytical procedure. Environmental impact levels progress from green through yellow to red, corresponding to low, moderate, and high impact respectively (***Płotka-Wasylka, J. et al., 2018).***

INSTALLATION----SOFTWARE LINK TO ACCESS "GAPI"

https://mostwiedzy.pl/en/justyna-plotka-wasylka,647762-1/gapi

This URL is generally referenced as the tool location for generating GAPI charts.

STEPS TO ACCESS "GAPI' TOOL

❖ Open Web Browser

- ❖ Download GAPI Excel tool using the link https://mostwiedzy.pl/en/justyna-plotka-wasylka,647762-1/gapi
- ❖ Open GAPI file
- ❖ Define analytical method and evaluate each method step
- ❖ Assign green/yellow/red codes
- ❖ Generate GAPI pictogram
- ❖ Interpret environmental impact

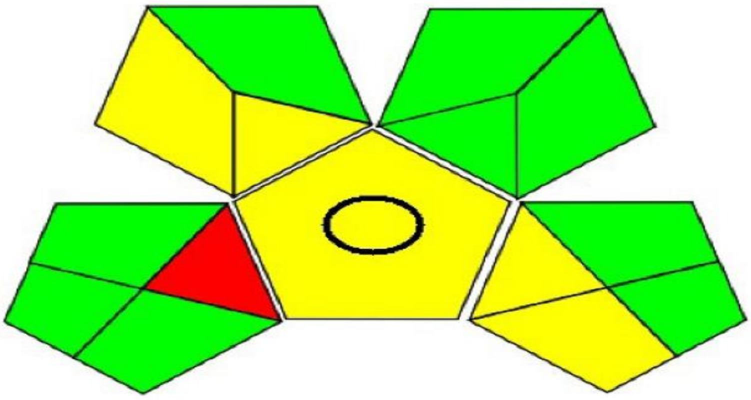

Figure 6: Pictogram of GAPI (*Płotka-Wasylka, J. et al., 2018*)

ADVANTAGES OF GAPI

GAPI functions as a straightforward GAC metric that delivers both qualitative and quantitative information regarding the greenness of analytical procedures(***Yin, L. et al., 2024***). It offers a rapid, high-level overview of the environmental profile of each step in the analytical methodology, supporting evaluation and optimization efforts to reduce environmental impact ***(Mansour, F. R. et al., 2024).***

LIMITATIONS OF GAPI

A notable limitation of GAPI is that it does not produce a single numerical total score for each procedure, which can limit direct quantitative comparisons between methods ***(Mansour, F. R. et al., 2024).***

5) COMPLEX Green Analytical Procedure Index(COMPLEXGAPI)

ComplexGAPI represents an extension of the original GAPI tool, developed in 2021 by *Plotka-Wasylka* and *Wojnowski* (***Płotka-Wasylka, J. et al., 202***1). The extended format incorporates an additional hexagonal component that enables evaluation of parameters not covered by the original GAPI, including extraction efficiency, temperature, reaction duration, chemical health and safety hazards, instrument setup requirements, energy demands, occupational hazards, and the purity of final products ***(Kaya, S. I. et al., 2024).***

INSTALLATION---SOFTWARE LINK TO ACCESS "COMPLEXGAPI" TOOL
https://mostwiedzy.pl/complexgapi

STEPS TO ACCESS COMPLEXGAPI TOOL

- ❖ Open Web Browser
- ❖ Download ComplexGAPI Tool
- ❖ Open Tool in Excel / Software
- ❖ Define Complex Analytical Workflow
- ❖ Break Method into Sub-Processes
- ❖ Assess Environmental Impact of Each Step
- ❖ Generate ComplexGAPI Pictogram and then interpret & optimize method

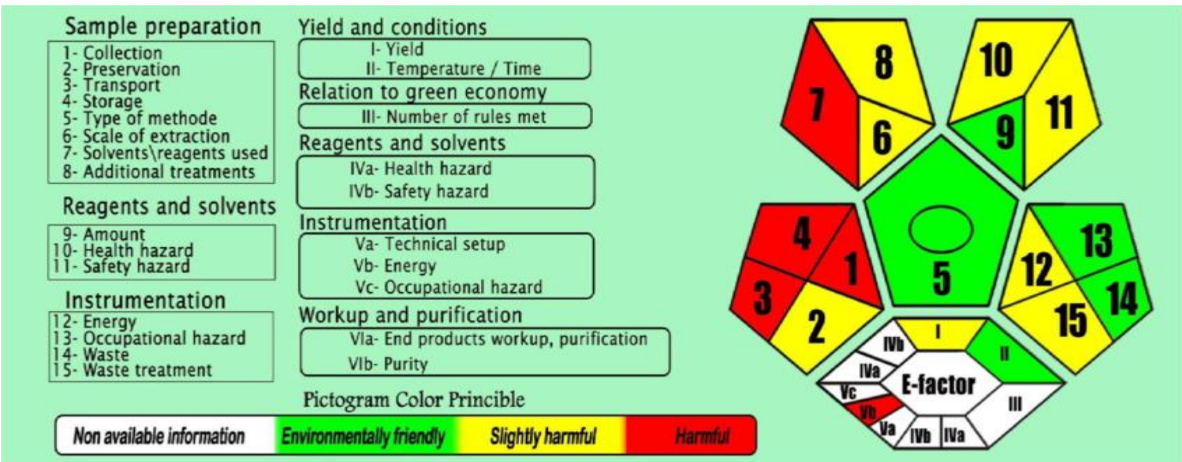

Figure 7: Pictogram of ComplexGAPI(*Płotka-Wasylka, J. et al., 202*1)

6) Modified Green Analytical Procedure Index (MoGAPI**)**

The Modified Green Analytical Procedure Index (MoGAPI) was introduced in 2024 to address certain limitations identified in the original GAPI tool ***(Mohr, A. et al., 2025)***.

Proposed by *Plotka-Wasylka*, the MoGAPI employs a color-coded pictogram in red, yellow, and green to represent high, moderate, and low environmental impact across the key stages of an analytical method. Critically, in addition to the characteristic GAPI pictogram, MoGAPI generates an overall score of up to 100 points, enabling quantitative comparative assessment of method greenness ***(Pepakayala, S. et al., 2025; Kaya, S. I. et al., 2024).***

This MoGAPI tool will ensure a holistic greenness assessment of the methods, and the accompanying software will ensure easier and faster application. In the future, this MoGAPI tool, along with its user-friendly software, will undoubtedly prove to be an invaluable resource for researchers and scientists who wish to develop and apply greener analytical methodologies. The continued use and application of this tool will pave the way for the larger goals of sustainability and environmental protection. The application of this new metric to different analytical methodologies and techniques will be the focus of our future work***(Mansour, F. R. et al., 2024).***

INSTALLATION---SOFTWARE LINK TO ACCESS (MoGAPI)

The software used to calculate the score and to generate the MoGAPI assessment is freely available (open source) at http://bit.ly/MoGAPI.

Steps to access “MoGAPI” tool

- ❖ Open Web BrowserGo to bit.ly/MoGAPI
- ❖ Download MoGAPI Software
- ❖ Install / Extract Tool
- ❖ Launch MoGAPI
- ❖ Enter Analytical Method Data
- ❖ Assign Scores to Parameters
- ❖ Generate MoGAPI Chart & Score
- ❖ Save/ Compare Results

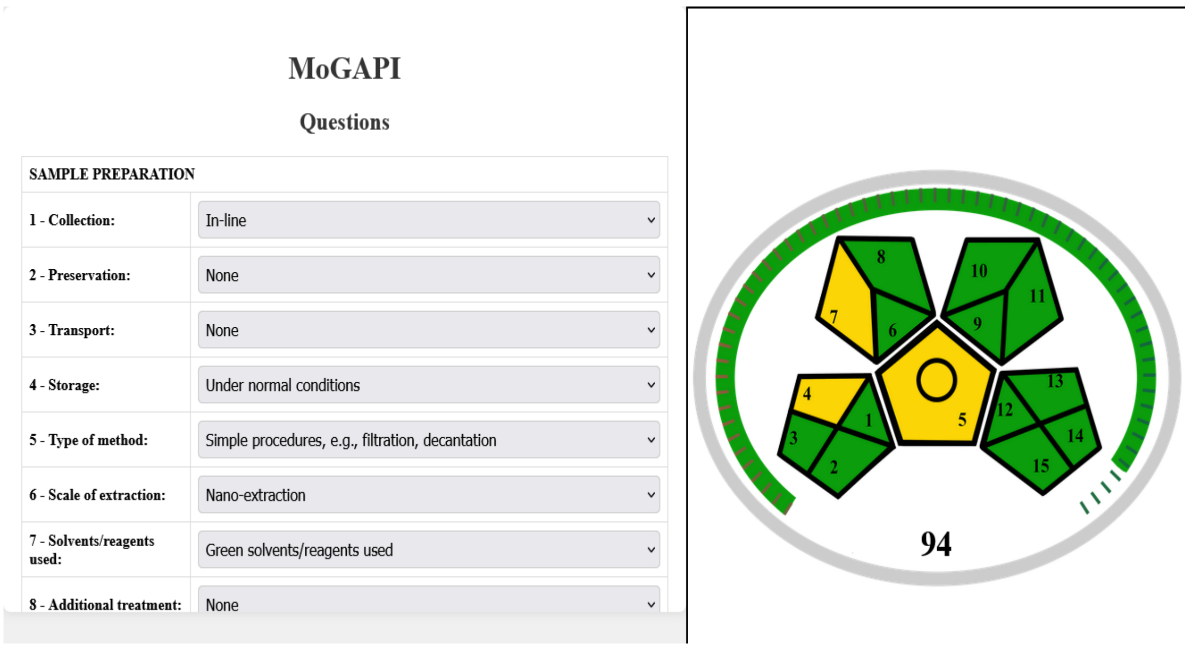

Figure 8: MoGAPI visualization of greeness score.

Table 2: MoGAPI Parameters Description: *(Mohr et al., 2025).*

			Color (Points)		
Category	**No.**	**Subsection**	**Green (3)**	**Yellow (2)**	**Red (1)**
Sample handling	1	Collection	In-line	On-line or at-line	Off-line
	2	Preservation	None	Chemical or physical	Physicochemical
	3	Transport	None	Required	–
	4	Storage	None	Normal conditions	Special conditions
Method type	5	Direct or indirect	No sample preparation	Simple procedures	Extraction required
Sample preparation	6	Scale of extraction	Nano	Micro	Macro
	7	Solvents/reagents used	None	Green solvents/ reagents	Non-green solvents/reagents
	8	Additional treatments	None	Simple	Advanced
Reagents and solvents	9	Amount	< 10 mL (< 10 g)	10 – 100 mL (10 – 100 g)	> 100 mL (> 100 g)
	10	Health hazard (NFPA health hazard score)	0 or 1	2 or 3	4
	11	Safety hazard (NFPA flammability or instability score)	0 or 1	2 or 3	4
Instrumentation	12	Energy	≤ 0.1 kWh per sample	≤ 1.5 kWh per sample	> 1.5 kWh per sample
	13	Occupational hazard	None (Hermetic sealing)	–	Vapors to the atmosphere
	14	Waste	< 1 mL (< 1 g)	1 – 10 mL (1 - 10 g)	> 10 mL (> 10 g)
	15	Waste treatment	Recycling	Degradation, passivation	No treatment

ADVANTAGES OF MoGAPI

Its user-friendly interface makes it a valuable resource for researchers working to develop and implement more sustainable analytical methods ***(Mansour, F. R. et al., 2024).***

The tool offers a clear visual representation of the environmental contribution of each analytical step, facilitating rapid identification of weaknesses and enabling straightforward method comparisons even when procedural steps differ substantially between methods. By providing dedicated software for direct data input and pictogram generation, MoGAPI allows for a faster and more precise assessment of method greenness ***(Mohr, A. et al., 2025).***

7) ComplexMoGAPI(Complex Modified Green Analytical Procedure Index)

ComplexMoGAPI represents the most advanced iteration of the MoGAPI tool, offering a more comprehensive evaluation process that yields more precise total scores through detailed calculation steps. The method comparison capability is enhanced relative to earlier tools, enabling a thorough assessment of the green profiles of analytical procedures***(Kaya, S. I. et al., 2024).***

INSTALLATION---SOFTWARE LINK TO ACCESS (MoGAPI)

This software is available as an open source on bit.ly/ComplexMoGAPI

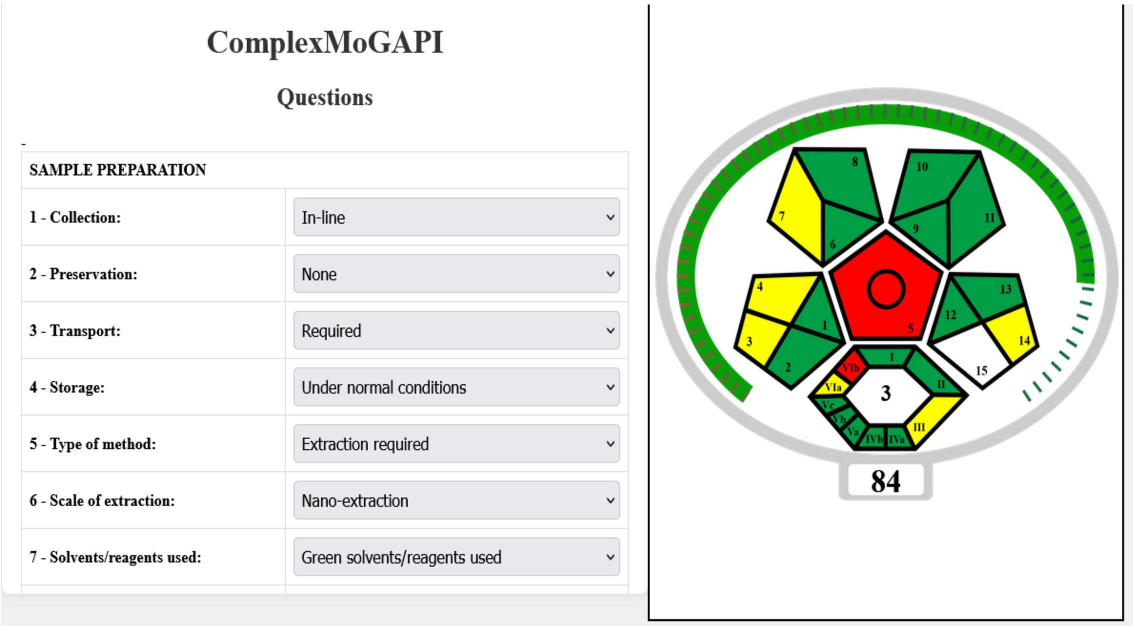

Figure 9: ComplexMoGAPI visualization of greeness score.

DISCUSSION

The theoretical and practical foundations of green extraction are built upon the six principles established by Chemat and colleagues, which emphasize the use of renewable plant resources, environmentally benign solvents, reduced energy consumption, production of valuable co-products rather than waste, simplified processing steps, and the generation of safe, high-quality extracts ***(Chemat.F, et al., 2012).*** Complementing these principles, the adoption of green solvents such as water, supercritical carbon dioxide, ionic liquids, and bio-based solvents has emerged as a defining characteristic of environmentally responsible phytochemical extraction. ***(Martins, R. et al., 2023).***

The integration of computerized greenness evaluation platforms has significantly advanced the capacity to assess and refine green extraction processes. Advanced metrics and software tools including GET, Path2Green, AGREE, AGREEprep, GAPI, ComplexGAPI, MoGAPI, and ComplexMoGAPI collectively enable systematic and quantitative evaluation of analytical and extraction methodologies. These platforms employ visual pictograms, numerical scoring systems, and sustainability indices to assess parameters such as solvent toxicity, energy consumption, waste generation, process safety, and environmental impact. By facilitating rapid comparison and optimization of extraction methodologies, these software-based evaluation systems advance the development of more sustainable and environmentally responsible analytical protocols **(*Kaya, S. I. et al., 2024*).**

Collectively, the convergence of green extraction strategies with computerized greenness assessment tools represents a significant advancement in natural product research, enabling the sustainable recovery of phytochemicals in alignment with global environmental protection goals and green analytical chemistry principles.

CONCLUSION

The growing global emphasis on sustainability has stimulated the development and adoption of green extraction techniques for the recovery of plant-derived bioactive compounds. Compared to classical approaches, modern techniques such as ultrasound-assisted and microwave-assisted extraction offer measurable advantages including reduced solvent consumption, shorter processing times, improved efficiency, and lower environmental footprint. These methods adhere to the principles of green chemistry and enable the extraction of herbal actives using eco-friendly solvents and advanced technologies including supercritical fluids, microwaves, and ultrasound, without compromising the potency of the extracted material.

Greenness metrics provide a structured and scientifically rigorous approach to evaluating the environmental performance of extraction methods by systematically assessing solvent toxicity, energy demands, waste generation, and process efficiency. This evaluation framework assists in identifying the most environmentally preferable techniques for both research and industrial applications.

The integration of green extraction technologies with quantitative greenness metric assessments supports the broader objective of sustainable phytochemical research. Future efforts should be directed toward the optimization of extraction conditions, development of novel green solvents, and standardization of assessment tools to ensure consistent, efficient, and environmentally responsible extraction practices across all research and industrial contexts.

REFERENCE

1. *Dhanani, T. et al., (2015)*. Comparison of green extraction methods with conventional extraction method for extract yield, L-DOPA concentration and antioxidant activity of *Mucuna pruriens* seed. *Green Chemistry Letters and Reviews*, 8(2): 43–48. https://doi.org/10.1080/17518253.2015.1075070
2. *Majid, I. et al., (2023).* Recent insights into green extraction techniques as efficient methods for the extraction of bioactive components and essential oils from foods. *CyTA – Journal of Food*, 21(1): 101–114. https://doi.org/10.1080/19476337.2022.2157492
3. *Martins, R. et al., (2023).* Green extraction techniques of bioactive compounds: A state-of-the-art review. *Processes*, 11(8): 2255. https://doi.org/10.3390/pr11082255
4. *Chemat, F. et al., (2012)*. Green extraction of natural products: Concept and principles. *International Journal of Molecular Sciences*, 13(7): 8615–8627. https://doi.org/10.3390/ijms13078615
5. *Kirusnaruban, K. et al,. (2025)*. Green extraction of wheat phenolic acids using microwave-assisted extraction. *Journal of Food Science*, 90: e70225.
6. *Usman et al., (2023).*, "Emerging trends in green extraction techniques for bioactive natural products." Processes, 2023; 11.12: 3444. https://doi.org/10.3390/pr11123444
7. *Švarc-Gajić et al., (2022)* "Recent advances in the development and application of green extraction techniques." Applied Sciences, 2022; 12.20: 10510. https://doi.org/10.3390/app122010510
8. *Janicka et al., (2022)*"Trends in the new generation of green solvents in extraction processes." Current Opinion in Green and Sustainable Chemistry, 2022; 37: 100670. https://doi.org/10.1016/j.cogsc.2022.100670
9. *Fan, L. et al., (2025).* Green extraction tree: A novel tool to greenness metric for green extraction of natural products. *ACS Omega*. https://doi.org/10.1021/acsomega.5c07167
10. 10.*de Souza Mesquita, L. M. et al., (2024).* Path2Green: Introducing 12 green extraction principles and a novel metric for assessing sustainability in biomass valorization. *Green Chemistry*, 26(19): 10087–10106. https://doi.org/10.1039/D4GC02512A
11. *Pepakayala, S. et al., (2025)*. Green and sustainable LC-APCI-MS/MS method for simultaneous quantification of genotoxic nitrosamines in antidiabetic medication: Sitagliptin. *BMC Chemistry*, 19: 135. https://doi.org/10.1186/s13065-025-01503-4
12. *Raj, B. et al., (2022).* Green extraction techniques for phytoconstituents from natural products. *IntechOpen*. https://doi.org/10.5772/intechopen.105088
13. *Mahdavi, R. et al., (2024).* Application of new green evaluation tools to assess the environmental impact of analytical procedures based on solid-phase microextraction techniques. *Green Analytical Chemistry*, 10: 100144. https://doi.org/10.1016/j.greeac.2024.100144
14. *Pena-Pereira, F. et al., (2020).* AGREE—Analytical GREEnness metric approach and software. *Analytical Chemistry*, 92(14): 10076–10082. https://doi.org/10.1021/acs.analchem.0c01887
15. *Pena-Pereira, F. et al., (2020)*. AGREE—Analytical GREEnness metric approach and software: Supporting information and software documentation. *Analytical Chemistry* (Supporting Information).
16. *Płotka-Wasylka, J.et al., (2018).* A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index. *Talanta*, 181: 204–209. https://doi.org/10.1016/j.jpha.2024.101013
17. *Yin, L. et al., (2024)*. Green analytical chemistry metrics for evaluating the greenness of analytical procedures. *Journal of Pharmaceutical Analysis*, 14(11): 101013. https://doi.org/10.1016/j.jpha.2024.101013
18. *Mansour, F. R. et al., (2024).* Modified GAPI (MoGAPI) tool and software for the assessment of method greenness: Case studies and applications. *Analytica*, 5: 451–457. https://doi.org/10.3390/analytica5030030
19. *Mohr, A. et al., (2025).* Overview of the greenness metrics used to evaluate analytical methods. *Brazilian Journal of Analytical Chemistry*. http://dx.doi.org/10.30744/brjac.2179-3425.RV-1-2025
20. *Pepakayala, S. et al., (2025)*. Green and sustainable LC-APCI-MS/MS method for simultaneous quantification of genotoxic nitrosamines in antidiabetic medication: Sitagliptin. *BMC Chemistry*, 19: 135.
21. *Martínez, J. et al., (2022)*. Green chemistry metrics: A review. *Processes*, 10(7): 1274. https://doi.org/10.3390/pr10071274
22. *Płotka-Wasylka, J. et al., (2021).* Complementary green analytical procedure index (ComplexGAPI) and software. *Green Chemistry*, 23(21): 8657–8665. DOI:10.1039/D1GC02318G
23. *Kaya, S. I. et al., (2024).* Green metrics and green analytical applications: A comprehensive outlook from developing countries to advanced applications. *Green Analytical Chemistry*, 11, 100159.https://doi.org/10.1016/j.greeac.2024.100159
24. *Mansour, F. R., et al., (2024). A total scoring system and software for complex modified GAPI (ComplexMoGAPI) application in the assessment of method greenness.* Green Analytical Chemistry, 10: 100126. https://doi.org/10.1016/j.greeac.2024.100126
25. *Wojnowski, W., et al., (2022). AGREEprep–analytical greenness metric for sample preparation.* TrAC Trends in Analytical Chemistry, 149, 116553. https://doi.org/10.1016/j.trac.2022.116553
26. *Pena-Pereira, F., et al., (2022). A tutorial on AGREEprep: An analytical greenness metric for*

sample preparation. Advances in Sample Preparation, 3: 100025. https://doi.org/10.1016/j.sampre.2022.100025

27. *Armenta, S., et al., (2019). Green extraction techniques in green analytical chemistry.* TrAC Trends in Analytical Chemistry, 116: 248–253. https://doi.org/10.1016/j.trac.2019.03.016