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Review Article

Green Extraction Technologies for Herbal Bioactive Compounds: Methods, Pharmaceutical Applications, Challenges, and Future Perspectives

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ABSTRACT

Herbal medicines are complex combinations of plants. The composition of the mixture depends on the part of the plant used, the type of plant, the conditions under which it was harvested, how it is processed and how it is extracted. Extraction is an important step to obtain phytochemicals for research and pharmaceutical development. While traditional techniques such as maceration, percolation, Soxhlet extraction and hydro distillation remain useful, they may involve a long processing time, large amounts of solvent, a lot of energy or heat exposure for delicate substances. Green extraction considers safer solvents, process intensifications, efficient energy utilization and responsible biomass management to enhance recovery and reduce occupational and environmental burdens. This review discusses the principles of green extraction and critically evaluates pressurized liquid extraction, enzyme-assisted extraction, supercritical fluid extraction, microwave-assisted extraction, ultrasound-assisted extraction, subcritical water extraction and natural deep eutectic solvents. Experimental optimization and comparative evaluation are considered along with important process variables including temperature, time, solvent composition, particle size, pH and solid to liquid ratio. Applications to alkaloids, polyphenols, terpenoids, essential oils, glycosides and other phytoconstituents are summarized and potential applications in herbal formulations and drug-delivery systems are discussed. Recent trends include hybrid technologies, environmentally benign solvent design, response-surface optimization and biorefinery techniques.

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There are still major hurdles to be overcome, including the need to differentiate laboratory bioactivity from therapeutic benefit, equipment costs, scale-up, solvent recovery, extract standardization and reproducibility. Instead of looking only at extraction yield, a green process should be assessed on the basis of product quality and safety but also on solvent, energy, waste and lifespan indicators.

INTRODUCTION

Medicinal plants are used in traditional healthcare and are a source of chemical diversity for pharmaceutical, nutraceutical and cosmetic research for a long time. Plant materials contain primary metabolites and a wide variety of secondary metabolites such as alkaloids, phenolic acids, flavonoids, tannins, terpenoids, saponins and glycosides. Besides being investigated for a variety of biological characteristics, these substances may be used as chemical markers for extract standardisation and plant identification. Species, plant part, growth conditions, season, harvesting, drying, storage and processing influence their concentration and occurrence [1–4,30].

Extraction is the process of transferring selected components from a plant matrix to an appropriate media. In addition, the total yield, selectivity, concentration of marker compounds, stability, residual solvents, impurities, and repeatability, all influence the quality of the final extract. However, some materials may be sensitive to solvents, extensive processing or heating. Conventional methods are still useful in laboratory and commercial settings. Green extraction technologies overcome these problems by combining safer solvents with techniques that enhance heat or mass transfer and minimise the wasteful use of resources [1–8].

It is a mistake to assume that if something is 'green' it is automatically safer or better for the environment. Equipment energy consumption, solvent production and recovery, downstream concentration, waste treatment, plant sourcing and process size can all alter the total environmental profile. In this paper we critically review the most commonly used green extraction technologies, their operational parameters, their applications on herbal ingredients and the hurdles to be overcome before pharmaceutical translation.

1.1 Overview of herbal medicine

Herbal medicines are defined by the World Health Organization as herbs, herbal materials, herbal preparations and finished products which contain plant-derived materials [9]. A botanical name alone cannot be used to guarantee consistent quality, due to their chemical complexity. Authentication, contamination control, appropriate extraction and chemical characterization can improve batch consistency and safety evaluation [9,10].

1.2 Importance of phytochemicals

Phytochemicals are important as possible active ingredients and as markers for comparison of extracts. Terpenoids are constituents of essential oils and other lipophilic extracts; glycosides and saponins exhibit different chemical properties; phenolics and flavonoids are often studied as part of antioxidant research; and alkaloids include compounds with well-known pharmacological activities. In the absence of adequate analytical and experimental data, the activity of a crude extract cannot be ascribed to a single compound. HPLC, LC–MS, GC–MS and validated spectrophotometric assays can aid in characterization when chosen for the analytes and matrix [3,10,11].

Table 1: Representative Phytochemical Groups and Factors Influencing Their Extraction.

Phytochemical group	Examples	Extraction considerations
Phenolic acids and flavonoids	Gallic acid, caffeic acid, quercetin, catechin	Often recovered with water, aqueous ethanol, UAE, MAE, PLE, or SWE; monitor oxidation and heat sensitivity.
Alkaloids	Berberine, quinine and other species-specific alkaloids	pH and ionization can strongly affect recovery; method selection should reflect structure and safety.
Terpenoids and volatile constituents	Selected monoterpenes, sesquiterpenes, essential-oil constituents	Volatility and thermal stability matter; hydro distillation or SFE may be appropriate for selected targets.

Phytochemical group	Examples	Extraction considerations
Glycosides and saponins	Species-specific cardiac, phenolic, or triterpenoid glycosides	Polarity and hydrolytic stability influence solvent, pH, and temperature selection.
Polysaccharides and other polar compounds	Plant gums, mucilage, selected carbohydrates	Aqueous or enzyme-assisted approaches may be suitable; viscosity and co-extraction can complicate purification.

1.3 The need for green extraction

Green extraction aims to obtain a chemically well-defined and safe result while minimizing the use of toxic solvents, process time, energy consumption and waste. These include replacing less suited solvents where practical, maximizing solvent-to-solid ratios, recovering solvents, effective energy delivery and, when safe, valorizing leftovers. Such objectives should be assessed in an objective way, a better crude yield or a shorter extraction time does not prove a reduced environmental impact [1,5-8].

2. Limitations of traditional extraction techniques

Standard methods are still useful as reference procedures, especially where low capital costs, established practices or availability of equipment are important. The effect of plant matrix, solvent polarity, temperature, particle size and extraction time are discussed [2,3,11].

2.1. Maceration

Maceration is the soaking of a comminuted plant material in a solvent of choice for a specified period of time, often with occasional mixing. It is easy to do and can be done at low temperatures which could help shield some thermolabile components. Some of its disadvantages are long contact times, possibly high solvent demand and the need for filtration and solvent removal. Also, sensitive components may change over time due to extended exposure to light or air [2, 11].

2.2 Extraction by Soxhlet

In a Soxhlet extractor the sample is flushed repeatedly with condensed hot solvent. It is effective at removing solvent soluble chemicals from dried powdered material. Important constraints are long cycles, continuous heating, use of solvents and possible thermal deterioration. It is a useful laboratory benchmark, but it may not be suitable for components that are extremely heat sensitive [2,12].

2.3 Percolation

Percolation is when a solvent is passed through a prepared bed of plant material. Liquid extracts and tinctures are made by percolation. Efficiency depends on wetting, packing density, particle size, solvent flow and contact time. Very small particles may block flow, but channel creation may lead to unequal extraction. Reproducibility requires control of the plant bed and process parameters, but it can be performed without continuous heating [3,11].

2.4 Hydro distillation

The volatile oils are usually obtained by hydro distillation in which the plant material is heated with water, the vapor condensed and the oil separated from the aqueous phase. It is based on known technology and does not require the use of an organic solvent in the distillation. Heat and water may be of importance, prolonged heating may alter or degrade some constituents, and the method is not suitable for many non-volatile, polar phytochemicals [2,18].

Table 2: Summary of Conventional Extraction Methods.

Method	Typical purpose	Strength	Main limitation
Maceration	Broad solvent extraction	Simple; can use mild temperature	Long duration and solvent use
Soxhlet	Solvent-soluble constituents from dried samples	Repeated contact with hot solvent	Energy demand and heat exposure

Method	Typical purpose	Strength	Main limitation
Percolation	Liquid extracts and tinctures	Continuous solvent contact	Packing and flow-related variability
Hydro distillation	Volatile oils	Established essential-oil method	Heat/water demand; limited to volatile constituents

3. Principles of green extraction

3.1 Green Chemistry and Safer Solvents

Green chemistry employs process and product design to reduce the use of harmful materials and to avoid waste. Solvent selection, energy efficiency, sustainable feedstocks, process safety, and waste prevention are all issues that are relevant to herbal extraction [13]. For polar or moderately polar molecules, water and aqueous ethanol are often used, while for some lipophilic compounds supercritical carbon dioxide can be helpful. Deep eutectic solvents are being investigated for bespoke extraction. Not all are suitable for every situation. Toxicity, flammability, biodegradability, solvent recovery, residual levels and compatibility with the planned dose form need to be assessed [1,5,7,8].

3.2 Waste, energy and solvent reduction

The goal is not just to minimize solvent volume regardless of outcome, but to use the least laborious procedure that gives acceptable recovery and quality. Optimization of the number of extraction cycles, solid to liquid ratio, solvent composition and downstream recovery can reduce inputs. The energy accounting should include heating, cooling, pumping, drying, evaporation and purifying, not only the extraction process. The remaining biomass can be considered for composting, bioenergy or further recovery of valuable compounds only after checking pollutants, residual solvents and biological safety [7,8,14].

3.3 Ecological supply of therapeutic plants

Sustainability begins before extraction. Botanical identification, traceable supply, responsible harvesting, conservation status, cultivation inputs, water use and community implications all affect the whole footprint. The requirements for regeneration may be different for collecting roots, bark, rhizomes or whole plants than for collecting leaves or flowers. Good agricultural and collection techniques and standardized growing enhance traceability and raw-material consistency. Laboratory yield alone is not an indication of sustainability without the consideration of quantity of plant material, resource use, waste and lifecycle implications [8,14,15].

4. Types of green extraction technologies

Methods used in green extraction technologies include physical, chemical or biological methods. A process is selected based on the target compounds, matrix, intended use, available equipment, safety considerations, and downstream purification, as these are complementary and not interchangeable [4–8,16].

4.1 Ultrasound assisted extraction (UAE)

The UAE is used to the liquid-solid system of acoustic energy. The formation and collapse of cavitation bubbles create local forces that damage plant tissues, increase mass transfer and promote solvent penetration. UAE is used for some polyphenols, flavonoids, pigments and other compounds of plant matrices. Equipment can often be cheaper than high pressure systems and can speed up extraction and possibly reduce the need for solvent. Frequency, amplitude, temperature, solvent and size of plant particles [4–6,18] influence heating, oxidation or degradation by excessive power or extended treatment.

4.2 Microwave assisted extraction (MAE)

MAE heats suitable solvents and wet plant tissues by microwave energy through dielectric interactions. Rapid heating can increase internal pressure and facilitate the release of intracellular chemicals. MAE can reduce solvent volume and processing time in suitable systems. However, care should be taken about uneven heating, temperature overshoot, solvent compatibility and thermolabile chemical degradation. Scaling-up and equipment design can also be challenging [2,4,5].

4.3 SFE, or supercritical fluid extractor

SFE uses a fluid, typically carbon dioxide, that is above its critical temperature and pressure. Supercritical CO

2 has low viscosity and relatively high diffusivity and its solvent strength can be tuned by temperature and pressure. It can be useful for some oils, volatile components and lipophilic substances and CO2 can be removed from the extract by depressurizing. Pure CO2 is relatively non-polar, so more polar targets might need a different approach or a modification such as ethanol. High capital costs and the need for high pressure equipment are significant barriers [2,4,16].

4.4 Pressurized Liquid Extraction (PLE)

PLE utilizes a liquid solvent at high temperature and sufficient pressure to maintain the liquid phase. The pressure is regulated to ensure uniform contact with the matrix, and higher temperatures can improve solubility and mass transfer. Suitable solvents can be ethanol, water and other solvents. PLE can be fast and automated but equipment can be costly and high temperatures can change delicate chemicals. The environmental assessment should include cooling, solvent recovery and downstream concentration [3, 5, 6].

4.5 Enzyme-assisted extraction (EAE)

In EAE, plant cell-wall structures are degraded using enzymes such as cellulases, pectinases and hemicelluloses to improve the accessibility of intracellular constituents. It may improve the recovery of tough plant matrices and can work under relatively mild conditions. The practical application may be limited by the cost of the enzyme, variation in activity, the pH and temperature requirements, reaction duration, and the removal of enzyme or reaction products downstream. The enzyme should be chosen to match the target and matrix [17].

4.6 Subcritical water extraction (SWE)

SWE uses pressurized liquid water at temperatures higher than the normal boiling point, but below the critical temperature of water. The polarity of water varies with temperature and so certain chemicals can be separated from water if they are less soluble at room temperature. SWE can reduce the need for organic solvents but the requirements for high pressure equipment and for heating must be taken into consideration. Conditions need to be optimized for the target chemicals as high temperatures can potentially cause hydrolysis or degradation [18,28].

4.7 Natural deep eutectic solvents (NADES)

The specific combination of hydrogen-bond donors and acceptors results in a liquid with a lower melting point than the individual constituents, which are called NADES. Typical constituents are organic acids, sugars, polyols, amino acids, betaine and choline chloride. Low volatility may reduce some solvent losses, and composition can be altered to solubilize specific plant metabolites. However, the recovery of the target from the solvent can be difficult, dilution can change the properties of the solvent and viscosity can slow down the mass transfer. Toxicological and residual solvent evaluation is still needed; “natural” origin does not guarantee non-toxicity, biodegradability or medicinal acceptability [19–21].

Table 3: Green Extraction Technologies: Mechanisms, Strengths, and Limitations.

Technology	Main mechanism	Potential strengths	Limitations / controls
UAE	Acoustic cavitation	Rapid mass transfer; moderate equipment needs	Power and temperature control; oxidation risk
MAE	Dielectric heating	Rapid heating; shorter processing in suitable matrices	Hot spots; solvent compatibility; scale-up
SFE	Supercritical fluid solvation	Adjustable selectivity; low residual CO_2 after depressurization	High-pressure equipment; limited polarity of pure CO_2
PLE	Hot pressurized liquid	Fast, controlled and potentially automated	Thermal stability; pressure-rated equipment
EAE	Enzymatic cell-wall breakdown	Mild conditions; selective matrix disruption	Enzyme cost and activity control
SWE	Hot compressed water	Reduced need for organic solvents	Heat demand; hydrolysis/ degradation risk

Technology	Main mechanism	Potential strengths	Limitations / controls
NADES	Tailored intermolecular interactions	Adjustable polarity; low volatility	Viscosity, recovery, toxicity and residual assessment

5. Factors affecting green extraction

5.1. Temperature and time of extraction

Temperature affects viscosity, diffusion, chemical stability and solubility. High heat can degrade, oxidize, hydrolyze or volatilize sensitive materials; however, moderate heating can improve mass transfer. • Extraction time affects contact and diffusion. • Yield generally increases early on and then levels off. • More treatment can waste energy and cause co-extraction and degradation. The time and the temperature should be optimized simultaneously for each plant-solvent-technology combination [5,18,22].

5.2 Solvent type and concentration

The polarity of the solvent must be similar to the target chemical. Many polar compounds can be recovered with water and aqueous ethanol but less polar systems or CO2 may be more suitable for lipophilic contents. In some substances, aqueous ethanol may combine enhanced solubility with tissue swelling. When selecting a solvent, one should take into account toxicity, flammability, renewability, recoverability, residual limitations, cost and downstream compatibility. The solvents used for analysis may not be suitable for extracts intended for human consumption [6–8,31].

5.3 pH, solid-liquid ratio and particle size

Small particles are good for surface area and for diffusion distances. Very small powders may agglomerate, interfere with filtration, increase suspended solids and require more energy for grinding. pH can affect the ionization, solubility and stability. Hydrolysis or other changes may be encouraged by high pH. In enzyme-assisted processes, pH must also be suitable for enzyme activity. The ratio of solid to liquid impacts wetting, concentration gradients, solvent saturation and downstream evaporation. Studies should adequately report the particle-size range, pH and ratio (e.g., grams of dry plant material per milliliters of solvent) [3,18,22].

5.4 Optimization and Replicability

Defined response, for example, target-marker recovery, extract yield, chemical fingerprint, or a validated biological endpoint, should be the first step in optimization. Design of experiments (DoE) or response-surface methodology (RSM) can be used to screen and optimize significant factors, including central composite or Box-Behnken designs where appropriate. The models have to be tested with residuals and confirmation studies. A high coefficient of determination does not prove predictive validity. Plant part, moisture status, particle size, solvent composition, ratio, pH, equipment settings, temperature, time, yield calculation, analytical method and repeat variability should be reported [22, 23].

6. Comparison of Traditional and Environmentally Friendly Extraction Techniques

Green technologies can improve selectivity, speed up processing, or improve mass transfer, but the extent to which they do so is a function of the matrix and the procedure. Conventional technologies may be competitive, if a mature process has been previously demonstrated or if they provide sufficient recovery with low-cost equipment. The starting material, target chemical, analytical endpoint and reporting basis should be the same in the comparisons. Crude yield should not be confused with medicinal efficacy or recovery of the intended constituent [1–8].

Table 4: Conventional and Green Extraction: A Critical Comparison Framework.

Criterion	Conventional methods	Green / intensified methods	What a fair comparison should report
Yield and selectivity	Can provide adequate yield; often less selective without process tuning	May improve release or selectivity for selected targets	Crude yield plus target-marker content and chemical profile

Criterion	Conventional methods	Green / intensified methods	What a fair comparison should report
Processing time	Maceration may be prolonged; Soxhlet uses repeated heating cycles	UAE/MAE and some pressurized methods can be faster	Total batch time, including preparation and cleaning
Solvent use	May require high solvent-to-solid ratios	Can reduce solvent demand in optimized applications; some new solvents are difficult to recover	Solvent volume per mass of plant and solvent recovery rate
Energy	Heating, reflux, evaporation, and drying can dominate	Potential process intensification; pressure, microwave, or ultrasound equipment also consumes energy	Energy per unit of standardized extract, including downstream steps
Cost and scale	Low capital cost for simple methods; productivity may be low	Specialized equipment can increase capital and maintenance cost	Capital, operating, labor, maintenance, throughput, and product value
Environmental profile	Depends on solvent, waste, and energy management	Potential improvement but not guaranteed	Lifecycle boundary, hazard, emissions, water, waste, and biomass sourcing

6.1 Environmental Impact Assessment

For comparisons in the environmental field the functional unit and the system boundary should be defined, e.g. energy and solvent consumption per gram of marker standardized extract. Relevant indicators are solvent hazard, solvent recovery, water use, power and heat, greenhouse gas emissions, waste production, demand on plant material and downstream purification. Life-cycle assessment can bring out trade-offs not apparent from the extraction yield alone. It is not certain that all alternatives are better than a procedure which uses a benign solvent but requires a lot of evaporation [7,8,14,15,32].

7. Herbal medicine applications

7.1 Alkaloid

Alkaloid extraction is greatly dependent on ionization and chemical structure. Acid–base environments can change solubility and phase distribution, but extreme pH may change sensitive molecules or require additional purification steps. Some alkaloids may be extractable using UAE, MAE, PLE, and custom solvent systems; the choice should be based on analyte-specific recovery, purity, stability, and residual-solvent constraints. Alkaloids may be pharmacologically potent [3,5,11], thus accurate identification and safety evaluation based on the dose are important.

7.2 Flavonoids and polyphenols

Phenolic acids and flavonoids are widely studied in the research of plant extracts. Aqueous ethanol, UAE, MAE, PLE, SWE and NADES can be helpful depending on the polarity, matrix and stability. The extraction conditions might impact the individual chemical profile, as well as the global phenolic or flavonoid assay results. For a particular marker, chromatographic confirmation is preferred. Colorimetric total-content assays are useful screening tools but do not identify individual molecules and may be affected by interfering compounds [4–8,18–21].

7.3 Terpenoids and essential oils

Volatile oils and lipophilic terpenoids can be extracted by hydro distillation, SFE and other methods which depend on volatility and thermal stability. Hydro distillation is still the most common way to extract essential oils, but SFE can allow selective extraction of some non-polar constituents. This is because the final profiles can be function of temperature, pressure, solvent and processing time, which ultimately influence recovery and possible transformation. Comparison must include total oil yield as well as composition [2,18].

7.4 Other phytoconstituents and glycosides

Glycosides, saponins, polysaccharides and other polar substances may need aqueous or aqueous-organic systems. Recovery is influenced by pH, hydrogen

bonding, hydrolytic stability and matrix binding. While SWE or PLE may be appropriate for some targets, enzyme-assisted extraction may provide increased access to chemicals entrapped within plant structures if degradation is controlled. Because of their chemical diversity no single approach should be used for all members of these classes [3,5,17,18].

Table 5: Illustrative Plant-Material and Target-Compound Pairings for Method Selection. Examples Are Not Universal Prescriptions; Plant-Specific Experimental Validation Is Required.

Plant / material example	Target class	Methods worth evaluating	Evidence and interpretation note
Tea leaves and other phenolic-rich botanicals	Catechins and other polyphenols	UAE, MAE, PLE, SWE, aqueous ethanol	Compare individual markers and degradation, not only total phenolic content.
Aromatic herbs	Essential oils and volatile terpenoids	Hydro distillation, SFE, selected intensified methods	Report oil composition and changes in volatile profile.
Alkaloid-containing medicinal plants	Species-specific alkaloids	pH-controlled solvent extraction, UAE, MAE, PLE	Report ionization conditions, purity, and analyte-specific recovery.
Polysaccharide-rich plant materials	Mucilage, gums, selected polysaccharides	Aqueous extraction, EAE, selected SWE conditions	Viscosity and co-extracted solids can complicate downstream processing.
Complex herbal mixtures	Multiple marker compounds	Sequential or hybrid extraction after screening	Validate each marker and confirm that extraction does not distort the intended profile.

8. Pharmaceutical applications of green-extracted compounds

8.1 Antioxidant, antimicrobial and anti-inflammatory research

Plant chemicals extracted with green solvents are often tested on inflammatory models, antibacterial assays and in vitro antioxidant assays. Assay results are affected by concentration, solvent residues, test design, and extract composition; however, these assays can be helpful for comparing extracts and generating hypotheses. Antioxidant capacity determined by a chemical assay alone cannot demonstrate clinical antioxidant benefit. In vitro antibacterial activity also does not prove treatment is safe or effective in humans. Claims should be restricted to the experimental design, with reproducible analytical data and appropriate controls [10,24,29].

8.2 Herbal formulation development

Standardized extracts may be used in the manufacture of tablets, capsules, granules, oral liquids, gels, creams or ointments provided their physicochemical characteristics are suitable for the dosage form. Characterization of marker content, residual solvents, moisture, microbiological quality, pollutants, stability and excipient compatibility is required for development. Drying and concentration may be important processes as they can change oxidation sensitive or thermolabile components. Therefore, the optimization of the extraction should not be aimed at the maximization of the crude yield, but should also consider the characteristics required for the final formulation [10,23,25].

8.3 Drug-delivery systems

Specific herbal components can be incorporated into nanoparticles, liposomes, phytosomes, nano emulsions or controlled-release systems in an effort to solve problems concerning solubility, stability or transport. These methods are not necessarily automatically enhancing clinical performance. Validation for particle size, loading, release, stability, residual materials, toxicity and reproducibility are required. Formulation-specific studies are needed to evaluate whether or not a delivery platform confers significant advantages over traditional formulation, and quality of the initial extract is still paramount [24, 25].

8.4 Standardization and quality control

Quality control should include chemical characterization, appropriate performance standards, botanical authenticity, and testing for contaminants. Chromatographic fingerprints and measurement of some markers may help in batch comparison. When a process is to be scaled up, critical material characteristics and process parameters should be defined and the extraction procedure should be verified against predefined quality standards. Quality-by-design and DoE ideas can be linked to material variability, process conditions and product quality but require the backing of the necessary analytical data [10,23,25,26].

9. Recent advances in green extraction methods

9.1 Hybrid and sequential technology

Hybrid techniques such as a deep eutectic solvent with an improved extraction method, a microwave with a pressurized liquid or ultrasound with a solvent system combine complementary mechanisms. By sequential extraction of compounds having different polarity, different phases can be obtained. While these techniques can lead to improved recovery or reduced processing times for some matrices, the added complexity could lead to increased equipment needs, energy consumption, problems with solvent recovery, and validation burden. Benefits [5,16,20,27] should be shown using a relevant single-method comparator.

9.2 Green Solvent Development

Investigations are underway into aqueous ethanol, bio-based solvents, deep eutectic solvents and tailor-made solvent combinations. The toxicity, environmental fate, renewability, viscosity, extraction performance, separation and recovery, and suitability for the intended use should be considered when evaluating a solvent in medicine. Separation of analytically useful solvent mixes from an extract may be difficult or the chemicals may remain in the solvent, limiting their utility. Safety and residual assessment should accompany extraction-performance investigations [7,19–21].

9.3 Integration and optimization of analytical processes

DoE and RSM can be helpful for multi-response optimization and modelling of interactions between the variables of the extraction. Modern analytical methods such as HPLC, LC-MS, GC-MS and chemical fingerprinting may be combined to monitor marker recovery and unwanted changes. Examples of useful optimization responses include yield, marker concentrations, selectivity, energy consumption, solvent usage, waste, and product stability. In many cases, multi-objective optimization gives more information than just selecting the condition with the highest crude yield [22, 23, 26].

9.4 Circular technologies and biorefineries

A biorefinery approach seeks to recover more than one useful product from medicinal-plant biomass by using a planned sequence of processing steps and minimizing avoidable waste. After the target bioactive fraction has been extracted, the remaining biomass may be assessed for secondary recovery of suitable constituents such as fibres, polysaccharides or other value-added fractions. Material that is not suitable for further recovery may be considered for an appropriate end use, such as composting or bioenergy, only after its composition and safety have been evaluated. Reuse must take account of residual extraction solvents, contaminants, degradation products and microbiological quality, as well as the requirements of the intended end use. A circular process should therefore be supported by a documented mass balance, material-flow data, solvent and energy accounting, and techno-economic and lifecycle assessment. Spent biomass should not be assumed to be safe, reusable or economically valuable without this evidence [14,15,27].

Table 6: Selected Recent Directions and Evidence Required for Translation.

Recent direction	Potential contribution	Evidence still needed
Hybrid extraction	Combines mechanisms to improve mass transfer or selectivity	Direct comparison, energy accounting, and reproducibility
NADES and alternative solvents	Tailored solubility and reduced volatility	Toxicity, recovery, residual limits, viscosity, and scale-up

Recent direction	Potential contribution	Evidence still needed
DoE / RSM optimization	Identifies factor interactions and multi-response optima	Model validation, confirmatory experiments, and transparent reporting
Biorefinery integration	Sequential recovery of primary bioactives and suitable secondary fractions from plant biomass; may reduce avoidable waste	Mass balance and material-flow data; residue identity and safety; residual-solvent and contaminant testing; energy/solvent accounting; techno-economic and lifecycle assessment

Table 7: Workflow for Green Extraction and Circular Biomass Utilization.

Stage	Core activity	Quality / sustainability checkpoint
1. Raw material	Authenticate plant; record plant part, origin, harvest and storage	Identity, traceability, moisture, contaminants
2. Preparation	Dry or condition appropriately; mill and define particle size	Avoid heat damage; record particle-size range
3. Method selection	Match target chemistry with solvent and technology	Safety, solvent hazard, equipment and intended use
4. Optimization	Study time, temperature, pH, ratio, power/pressure and solvent composition	DoE/RSM where appropriate; replicated confirmation
5. Extraction and separation	Extract and separate the target fraction; filter/centrifuge; recover solvent where feasible; segregate and record spent biomass	Record mass balance, solvent recovery, process inputs and waste streams
6. Residue assessment and valorization	Characterize spent biomass; assess secondary recovery of suitable fractions or an appropriate end use	Check residual solvents, contaminants and microbiological safety; document material flows and validate the proposed end use
7. Characterization	Quantify markers; fingerprint extract; assess relevant bioactivity	Validated analytical method; distinguish in-vitro from clinical evidence
8. Standardization and formulation	Set specifications and test stability/compatibility	Batch consistency, residual solvents, microbial quality
9. Scale-up review	Assess economics, energy, emissions, throughput and lifecycle impact	Pilot validation and documented process control

10. Difficulties and constraints

10.1 Scale-up and equipment cost

MAE and some hybrid platforms require certain equipment and process controls to be in place while SFE and PLE require pressure-rated systems. Heat transfer, cavitation, mixing, flow distribution, and mass transfer are scale-dependent, so laboratory performance does not necessarily carry over directly to larger vessels. Besides replicating laboratory extraction yield, scale-up should consider throughput, cleaning, maintenance, operator safety, batch consistency, solvent recovery and downstream processing [5,8,16,27].

10.2 Standardization and reproducibility of extraction

Even with the same extraction parameters, the final extract can be affected by plant-to-plant and batch-to-batch variation. So botanical authentication, controlled sourcing, defined plant parts, moisture and particle-size specifications, chemical fingerprints, and marker assays are crucial. Pharmaceutical translation studies that only report crude yield or total phenolic content may not be sufficient. Analytical techniques should be assessed for relevant performance characteristics and appropriate for the purpose [10,23,25].

10.3 Safety of solvents and stability of phytochemicals

Advanced technology and alternative solvents carry their own risks. Ethanol is flammable, water in high temperature can promote hydrolysis, ultrasound and microwave treatments can induce heating or oxidation and NADES components can be biologically active. We need to assess residual solvents, process pollutants and modifications to the chemical profile. Safety is determined by the final extract and the intended administration route, not solely by the reputation of the extraction solvent [7,19–21,24].

10.4 Evidence quality and regulatory translation

Direct comparison is complicated by the fact that many studies are laboratory scale and use different plant sources, solvents, analytical endpoints and reporting units. A higher yield or a stronger in vitro response does not show improved therapeutic efficacy. To translate, standardized extracts, reproducible manufacture, suitable toxicology, data on stability and, if therapeutic claims are intended, well-designed clinical research are required. Authors should separate exploratory findings from validated pharmaceutical outcomes [9,10,24,25].

Table 8: Key Barriers and Possible Mitigation Measures.

Challenge	Practical response
High capital / operating costs	Conduct process and techno-economic assessment early; compare with optimized conventional methods.
Difficult scale-up	Use pilot-scale studies and record engineering parameters, throughput, mixing and heat-transfer behavior.
Variable botanical raw material	Use authenticated, traceable materials and predefined incoming-material specifications.
Limited comparability	Report complete process settings, yield basis, marker recovery, replicates and analytical methods.
Solvent or extract safety	Assess hazards, residual levels, stability, contaminants and route-specific safety.
Overinterpretation of bioactivity	Separate chemical assay, in-vitro, in-vivo and clinical evidence explicitly.

11. Future perspectives

Future progress will depend on the integration of extraction science with analytical chemistry, process engineering, pharmaceutical development and botanical quality systems. More research should compare methods using the same batch of authenticated plant and common analytical outcomes. The recovery of the marker, solvent consumption, extract fingerprint, water use, energy utilization, waste and overall process time should all be reported. Wherever feasible, the lifecycle and techno-economic evaluation should be carried out sufficiently early to influence the method selection [5,7,8,14].

A second priority is standardization. The extraction procedures must be designed based on defined quality criteria like the content of markers, the impurity profile, stability, and suitability for the desired dosage form. Bridging laboratory work and manufacturing requires reliable analytical techniques, solvent recovery strategies, pilot scale validation and reliable raw material sourcing. More open reporting of negative or neutral results [10,23,25,26] could also prevent overestimating the benefits of a new technology.

Finally, in pharmaceutical research, the important biological and clinical evidence needs to be associated with the extraction results. Standardized extracts should be evaluated with appropriate controls, toxicological evaluation and well-planned trials before therapeutic claims are made. Claims about sustainability should also be based on measurable facts instead of adjectives like “natural,” “green” or “eco-friendly.”

CONCLUSION

Green extraction technologies offer practical alternatives for the recovery of particular bioactive chemicals from medicinal plants. UAE and MAE use acoustic or microwave energy to speed up mass transfer; SFE and PLE use controlled fluid properties; EAE uses

enzymatic modification of plant structures; SWE uses pressured hot water; and NADES provide adaptable solvent systems. Each approach has its pros and cons, and no technique is always better. The choice should consider target chemistry, botanical variability, compound stability, solvent safety, equipment, downstream recovery and expected product quality. Besides solvent, energy, waste, cost and lifecycle indicators, a comprehensive comparison should report marker recovery and chemical profile. However, green extraction should be standardized, reproducible, scalable, safe and have more robust pharmacological and clinical data before it can be converted into reliable herbal drugs.

REFERENCES

1. Chemat F, Abert Vian M, Cravotto G. Green extraction of natural products: concept and principles. Int J Mol Sci. 2012;13 (7):8615–8627. doi:10.3390/ijms13078615.
2. Azmir J, Zaidul ISM, Rahman MM, Sharif KM, Mohamed A, Sahena F, et al. Techniques for extraction of bioactive compounds from plant materials: a review. J Food Eng. 2013;117 (4):426–436. doi:10.1016/j.jfoodeng.2013.01.014.
3. Bitwell C, Sen IS, Chimuka L, Maseka KK. A review of modern and conventional extraction techniques and their applications for extracting phytochemicals from plants. Sci Afr. 2023;19:e01585. doi:10.1016/j.sciaf.2023.e01585.
4. Kumar M, Dahuja A, Tiwari S, Punia S, Tak Y, Amarowicz R, et al. Recent trends in extraction of plant bioactives using green technologies: a review. Food Chem. 2021;353:129431. doi:10.1016/j.foodchem.2021.129431.
5. Cannavacciuolo C, Pagliari S, Celano R, Campone L, Rastrelli L. Critical analysis of green extraction techniques used for botanicals: trends, priorities, and optimization strategies—a review. TrAC Trends Anal Chem. 2024;173:117627. doi:10.1016/j.trac.2024.117627.
6. Ameer K, Shahbaz HM, Kwon JH. Green extraction methods for polyphenols from plant matrices and their byproducts: a review. Compr Rev Food Sci Food Saf. 2017;16 (2):295–315. doi:10.1111/1541-4337.12253.
7. da Silva RF, Carneiro CN, de Sousa CBC, Gomez FJV, Espino M, Boiteux J, et al. Sustainable extraction bioactive compounds procedures in medicinal plants based on the principles of green analytical chemistry: a review. Microchem J. 2022;175:107184. doi:10.1016/j.microc.2022.107184.
8. Martins R, Barbosa A, Advinha B, Sales H, Pontes R, Nunes J. Green extraction techniques of bioactive compounds: a state-of-the-art review. Processes. 2023;11 (8):2255. doi:10.3390/pr11082255.
9. World Health Organization. Traditional, complementary and integrative medicine. Available from: https://www.who.int/health-topics/traditional-complementary-and-integrative-medicine. Accessed 19 Oct 2026.
10. World Health Organization. Quality control methods for herbal materials. Geneva: World Health Organization; 2011. Available from: https://www.who.int/publications/i/item/9789241500739.
11. Zhang QW, Lin LG, Ye WC. Techniques for extraction and isolation of natural products: a comprehensive review. Chin Med. 2018;13:20. doi:10.1186/s13020-018-0177-x.
12. Luque de Castro MD, García-Ayuso LE. Soxhlet extraction of solid materials: an outdated technique with a promising innovative future. Anal Chim Acta. 1998;369 (1–2):1–10. doi:10.1016/S0003-2670 (98)00233-5.
13. Anastas PT, Warner JC. Green Chemistry: Theory and Practice. New York: Oxford University Press; 1998.
14. Herrero M. Towards green extraction of bioactive natural compounds. Anal Bioanal Chem. 2024;416:2039–2047. doi:10.1007/s00216-023-04969-0.
15. Marcelino S, Gaspar PD, Paço A. Sustainable waste management in the production of medicinal and aromatic plants—a systematic review.

Sustainability. 2023;15 (18):13333. doi:10.3390/su151813333.

16. Rombaut N, Tixier AS, Bily A, Chemat F. Green extraction processes of natural products as tools for biorefinery. Biofuels Bioprod Biorefin. 2014;8:530–544. doi:10.1002/bbb.1486.
17. Puri M, Sharma D, Barrow CJ. Enzyme-assisted extraction of bioactives from plants. Trends Biotechnol. 2012;30 (1):37–44. doi:10.1016/j.tibtech.2011.06.014.
18. Pogorzelska-Nowicka E, Hanula M, Pogorzelski G. Extraction of polyphenols and essential oils from herbs with green extraction methods—an insightful review. Food Chem. 2024;460 (Pt 1):140456. doi:10.1016/j.foodchem.2024.140456.
19. Dai Y, van Spronsen J, Witkamp GJ, Verpoorte R, Choi YH. Natural deep eutectic solvents as new potential media for green technology. Anal Chim Acta. 2013;766:61–68. doi:10.1016/j.aca.2012.12.019.
20. Dai Y, Witkamp GJ, Verpoorte R, Choi YH. Natural deep eutectic solvents as a new extraction media for phenolic metabolites in Carthamus tinctorius L. Anal Chem. 2013;85 (13):6272–6278. doi:10.1021/ac400432p.
21. Dai Y, van Spronsen J, Witkamp GJ, Verpoorte R, Choi YH. Application of natural deep eutectic solvents for the extraction of bioactive plant secondary metabolites. Phytochem Anal. 2013;24 (6):619–628. doi:10.1002/pca.2434.
22. Sridhar A, Vaishampayan V, Senthil Kumar P, Ponnuchamy M, Kapoor A. Extraction techniques in food industry: insights into process parameters and their optimization. Food Chem Toxicol. 2022;166:113207. doi:10.1016/j.fct.2022.113207.
23. Weremfo A, Abassah-Oppong S, Adulley F, Dabie K, Seidu-Larry S. Response surface methodology as a tool to optimize the extraction of bioactive compounds from plant sources. J Sci Food Agric. 2023;103 (1):26–36. doi:10.1002/jsfa.12121.
24. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177. doi:10.3389/fphar.2013.00177.
25. International Council for Harmonisation. Pharmaceutical Development Q8 (R2). Geneva: ICH; 2009. Available from: https://www.ich.org/page/quality-guidelines.
26. Heng MY, Tan SN, Yong JWH, Ong ES. Emerging green technologies for the chemical standardization of botanicals and herbal preparations. TrAC Trends Anal Chem. 2013;50:1–10. doi:10.1016/j.trac.2013.03.012.
27. Capaldi G, Binello A, Aimone C, Mantegna S, Grillo G, Cravotto G. New trends in extraction-process intensification: hybrid and sequential green technologies. Ind Crops Prod. 2024;209:117906. doi:10.1016/j.indcrop.2023.117906.
28. Cheng Y, Xue F, Yu S, Du S, Yang Y. Subcritical water extraction of natural products. Molecules. 2021;26 (13):4004. doi:10.3390/molecules26134004.
29. Atanasov AG, Zotchev SB, Dirsch VM, Supuran CT. Natural products in drug discovery: advances and opportunities. Nat Rev Drug Discov. 2021;20:200–216. doi:10.1038/s41573-020-00114-z.
30. Won S, Kwon KH. Green technology for extraction of bioactive compounds from edible plants. J Oleo Sci. 2024;73 (10):1249–1265. doi:10.5650/jos.ess24162.
31. Chemat F, Abert Vian M, Ravi HK, Khadhraoui B, Hilali S, Perino S, Tixier AS. Review of alternative solvents for green extraction of food and natural products: panorama, principles, applications and prospects. Molecules. 2019;24 (16):3007. doi:10.3390/molecules24163007.
32. Capello C, Fischer U, Hungerbühler K. What is a green solvent? A comprehensive framework for the environmental assessment of solvents. Green Chem. 2007;9:927–934. doi:10.1039/B617536H.

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