



Review Article

RECENT ADVANCES IN MICROWAVE-ASSISTED EXTRACTION (MAE) OF MEDICINAL PLANTS: A REVIEW

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ABSTRACT

Since the last decade, there is enhanced interest for the use of Microwaves for the extraction (MAE) of the constituents of plant material. This review gives a brief theoretical background on MAE the principles and the types of instruments used have been presented. The main parameters like microwave power, extraction time, solvents, temperature and effect of stirring, etc., which influence the MAE have been discussed. Through numerous examples, it is demonstrated that this technique allows reduced solvent consumption and shorter extraction times, while the extraction yields of the analytes is equivalent to or even higher than those obtained with other extraction processes generally employed for extraction.

Keywords: Microwave-assisted extraction, conventional extraction, microwave energy, flavonoids, quinones, phenylpropanoids, coumarins.

INTRODUCTION

For thousands of years of herbal medicine have played a vital role in health care and avoidance of diseases¹. Latest years have shown a growing attractiveness and confidence in the use of herbal medicine worldwide. This may be because of the realization that current synthetic drugs have unsuccessful to provide a “cure all” assurance to most of the human diseases with often producing unwanted side effects².

Extraction is the elementary phase in phytochemistry research meanwhile the preparation of crude extracts from plants is the starting point for the isolation and purification of chemical ingredients existing in plants. Innovative extraction techniques containing microwave assisted extraction (MAE), pressurized solvent extraction (PSE) and supercritical fluid extraction (SCFE), have drawn significant research attention in the previous decade³. For the past 100 years, Soxhlet extraction has been the most appreciated among all other conventional methods. It serves not only as a technique for extraction of active constituents but also as a reference to equate newer extraction techniques³.

Soxhlet extraction has a shortcoming of having longer extraction period and also the extensive amount of heat energy necessary for its process. The procedure being time consuming results in more labor-intensive phases and general the number of samples that can be processed is reduced^{4,5}.

The extraction of secondary metabolites by microwave provides a massive scope of research consideration. This review principally deals with the application of microwave as an extraction tool for the extraction and isolation of secondary metabolites. Also, it offers a short theoretical background and the elementary principles of using microwave energy.

THE HISTORY OF MICROWAVE ASSISTED EXTRACTION

1975 Abu-Samra was the first researcher ever to use a microwave domestic oven in the laboratory, performing trace analysis of metals from biological samples⁶. The earliest studies concerning microwave extraction were by Ganzler in 1986. They used a microwave oven to heat biological samples and soil sample to extract organic compounds⁷. In 1991 Paré patented a method for the microwave extraction of natural products⁸.

These authors explored the use of microwave heating at raised temperatures and pressure for the extraction of additives from polyolefin. The MAE was performed with 30 mL of a mixture of acetone and n-heptane. They obtained 90-100% recoveries of the additives with extraction times of 3-6 min without degradation of the analytes at the elevated temperatures of the extraction. This compared kindly with the conventional 16h Soxhlet techniques⁹.

THE FUNDAMENTALS OF MICROWAVE ENERGY

Microwaves are non-ionizing electromagnetic waves of frequency between 300 MHz to 300 GHz or between wavelengths of 1 cm and 1m. They are positioned between the X- ray and infrared rays in the electromagnetic spectrum. Microwaves are made up of two oscillating perpendicular field's i.e. electric field and magnetic field and the former is responsible for heating¹⁰. Contrasting conventional heating which depends on conduction – convection phenomenon with ultimately much of the heat energy being lost to the environment, in case of MAE, heating occurs in a besieged and selective manner with practically no heat being lost to the environment as the heating occurs in a closed system. This distinctive heating mechanism can significantly reduce the extraction time as compared to Soxhlet extraction¹⁰.

ELEMENTARY PRINCIPLE

Mechanism of microwave extraction

As a result of a synergistic combination of two transport singularities: heat and mass gradients working in the equal direction in MAE, the procedure acceleration give a great extraction yield¹¹.

Through the extraction process, the recovery rate of the extract is not a direct function of time: the concentration of solute inside the solid varies, leading to unstable condition. Sequence of phenomenological stages must occur during the period of interaction between the solid-containing particle and the solvent effectuating the separation, containing (1) diffusion of the solvent into the solid matrix; (2) solubilization and/or breakdown of components; (3) transport of the solute out of the solid matrix; (4) relocation of the extracted solute from the external surface of the solid into the bulk solution; (5) movement of the extract with the solid; and (6) separation and release of the extract and solid⁸.

Mechanism of microwave heating

Energy transfer is the central characteristic of microwave heating. Usually, in heat transfer of the conventional procedure, the energy is transferred to the material by convection, conduction, and radiation phenomena finished the external material surface in the presence of thermal gradients. Dissimilarity, in MAE, the energy of the microwave is dispersed directly to materials through molecular- electromagnetic field interactions through transformations of electromagnetic energy into thermal energy¹².

The dielectric properties of materials depend on two factors. The first is ' ϵ ', the dielectric constant which designates the polarizability of the molecule in an electric field. The dielectric loss factor; ' ϵ'' ', measures the efficiency with which the absorbed microwave energy can be converted into heat. The ratio of the two terms is the dissipation factor, ' ϵ''/ϵ' ' ultrasonic extraction $\delta = \epsilon''/\epsilon'$ eq.

The material complex permittivity is related to the ability of the material to interact with electromagnetic energy, whereas ' ϵ' ' is the dielectric constant, and ' ϵ'' ' is the imaginary part. The dielectric constant determines how much of the incident energy is reflected at the air-sample border and how much enters the sample; the loss factor measures the efficiency of the absorbed microwave energy to be converted into heat¹³.

APPARATUSES AND EQUIPMENT

There are two kinds of commercially accessible MAE systems: closed extraction vessels and focused microwave oven¹⁴. Closed extraction vessel/ multimode are often used to extract plant secondary metabolites under great extraction temperature and pressure. It is economic in terms of solvent and is favorable to the extraction of the volatile mixtures¹⁵. Whereas in focused microwave assisted solvent extraction (FMASE), as the name indicates; one part of the extraction vessel covering the sample is focused for irradiation with microwave. Both the closed vessel type and the focused type are available commercially as multimode and single- mode or focused systems. A multimode system lets random spreading of microwave radiation within the microwave cavity, so every zone in the cavity and sample is irradiated evenly¹⁶.

Temperature control system

Temperature control is essential to optimize the extraction efficiency, avoid thermal degradation of the target analytes, and to provide reproducible operating conditions. This is achieved with a temperature measurement system that is microwave-transparent so it does not cause any self-heating. The temperature probe is inserted right into the control vessel to extend the temperature of the solvent -sample mixture. It is then used in a feedback control loop to adjust the microwave power output to achieve and sustain the operator-selected extraction temperature¹⁷.

Solvent safety features

Owing to the flammable features of many organic solvents, there is a chief safety issue when heating a solvent in a microwave field. This safety issue is overstated when heating these solvents in wraps vessels at temperatures up to 100 °C above their atmospheric boiling point. The microwave system should have fired safety structures, each acting as a holdup to prevent possible explosion from occurring inside the cavity. Apparatuses should be designed to eliminate possible explosion sources, to detect solvent escapes and to remove leaking solvent¹⁸.

ADVANTAGES AND DISADVANTAGES

The focal advantages of MAE over the conventional extraction techniques are that it reduces solvent depletion, it has a shorter operating time, it possesses temperately high recoveries, has a noble reproducibility and minimal sample manipulation for extraction procedure¹⁹.

MAE is suitable for the recovery of a vast array of compounds, and is recognized as a versatile and an efficient extraction technique of secondary metabolites from plants. MAE is relatively cost-effective when equaled to speed solvent extraction²⁰. The foremost advantage of MAE over ultrasonic-assisted extraction is its reduced extraction time. Yet, microwave irradiation can accelerate the chemical changes of some target secondary metabolites^{21, 22}, and other operational conditions (e.g., high extraction pressure) of MAE may modify the chemical structures of the target compounds, both of which might result in the reduction of extraction yield^{23,15}. During the extraction of flavonoids from *Acanthopanax senticosus* using closed extraction vessel, rutin in the crude extract was found to degrade when the pressure was over 300 kPa. The higher the pressure is, the faster the breakdown rate of rutin, hyperin and quercitrin²⁴.

Compared with UAE, apparatuses and equipment of MAE are more expensive and their operation is more difficult in many cases^{25,26}.

Furthermore, extraction efficiency of microwave technique may be very poor when whichever the aim compounds or solvent are nonpolar, or when the viscosity of solvent is extremely high^{27,28}.

In overall, MAE is not fit for the extraction of the thermally labile compounds²⁸.

ASPECTS TO CONSIDER WHEN USING THE MICROWAVE ASSISTED EXTRACTION METHOD

Extraction and mechanism of action

The optimization of MAE conditions has been studied in numerous submissions. The effectiveness of the process is rightly related to the operation conditions selected. Distinct attention

should be given to usually study parameters that may influence the performance of MAE such as solvent composition, solvent ratio, extraction temperature and time, microwave power, and the characteristics of the matrix its water content²⁹.

The select of solvent

In an experimental setup the choice of the solvent will be based upon the solubility of the wanted analyte, the solvent matrix interaction and the property of the solvent to absorb microwaves³⁰.

Microwave-power

The factors microwave power and irradiation times influence each other to a great extent. In order to optimize MAE process a combination of moderate power with longer coverage is generally selected. While with the use of high power there is related risk of thermal deterioration there are reports which shows that variable of power had no important effects on the yield of flavonoids³¹.

Application time

Time period of heating is another vital factoring that influences the extraction process of MAE. The amount of analyte extracted can be improved with an increase in the extraction time; however, there is an associated risk of degradation of thermo-labile components³².

Temperature

High-temperature extraction can be gainful with the resulting increase in solubility. This is because higher temperature causes increased intermolecular interactions within the solvent, giving rise to higher molecular motion which increases the solubility. The growing temperature may also cause a cellular pressure build up which may cause cell rupture and opening of the cell matrix, and as a result, increased components accessibility to be extracted into the solution³³.

Effect of stirring

The outcome of stirring is related to the mass transfer manner in the solvent phase. Therefore, balance between the aqueous and vapor phases can be achieved more rapidly. The use of agitation in MAE quickens the extraction by enhancing desorption and dissolution of active compounds bound to the sample matrix. Through stirring, the disadvantages of the use of low solvent-to-solid ratio can be reduced, together with the minimization of the mass transfer barrier created by the concentrated solute in a localized region resulting from insufficient solvent. It is possible to observe the difference between suspensions with and without stirring³⁴.

Effect of contact surface area and water content

The characteristics of the sample also affect the MAE process. It is recognized that in a higher contact surface area the extraction efficiency rises. Similarly, finer particles allow improved penetration of the microwave. On the other hand, very fine particles may stance some technical problems; so, filtration is applied to prepare the matrix³⁵.

In the preparation step the sample is grinded and homogenized to increase the contact area between the matrix and the solvent. The particle sizes are usually in the range of 100 mm to 2 mm. In some cases saturated of the dried plant material in the extracting solvent

before MAE has resulted in improved yield. This process is named pre-leaching extraction³⁵.

Impact of microwave on plant material

In order to provide evidence to elucidate the mechanism of MAE of effective components of plants, structural changes of vegetable samples after extraction were observed by light microscopy, scanning electron microscopy (SEM), transmission electron microscopy and atomic force microscopy³⁶⁻³⁸. The microstructure and ultrastructure of the samples of *E. breviscapus* processed by different extraction methods and the unprocessed samples were examined. Remarkably, microwave treatment disrupted the tissues of *E. breviscapus*. During the disruption process, a rapid exudation of chemical substances from the cells into surrounding extractant took place. On the contrary, the structures of the samples after heat-flux extraction were not considerably different from those of the unprocessed samples, and only few slight ruptures appeared on the surface of the samples after heat-flux extraction³⁶.

APPLICATIONS

Microwave Assisted Oil Extraction

Essential oils (Eos) of *Nigella sativa* L. seeds and its major active component, thymoquinone (TQ), possess a broad variety of biological activities and therapeutic properties MAE of the EO from *Nigella sativa* L. seeds and the antioxidant capacity of EO extracted by different methods were evaluated and the results showed that MAE method was a viable alternative to hydrodistillation (HD) for the EO extraction from *Nigella sativa* seeds due to the excellent extraction efficiency, higher TQ content, and stronger antioxidant activity³⁹.

In HD process, the heat transfer is principally executed by convection and conduction only, while in the procedure of MAE, it is implemented in three ways including convection, conduction and radiation¹⁰. Therefore, in MAE procedure, heat is generated from inside the glands as well as from the outside. When the glands were exposed to more acute thermal stresses and localized high pressures, as in the case of microwave heating, the pressure build-up inside the glands could have exceeded their capacity for expansion, and caused their rupture more quickly and completely than in conventional extraction^{37, 40}. After MAE, most of cells appeared completely disrupted explaining that all the cell walls are finally damaged and collapsed, and have resulted into undefined boundaries radical scavenging and antifungal activities of *Chaerophyllum acropodum* and *Oliveria decumbens* EOs extracted with microwave-assisted hydrodistillation (MAHD) were evaluated in comparison with the same EOs extracted by conventional HD. The final EO yields that were obtained using HD (after 150 min) and MAHD (after 45 min) were 1.72 and 1.67% for *C. macropodum* and 8.10 and 7.91% for *O. decumbens*, respectively. There were no notable differences between the finishing EO yields extracted with HD and MAHD, but MAHD could significantly reduce the duration of the extraction operation⁴⁰. Gas chromatography-Mass spectroscopy (GC-MS) analysis of EOs indicated that there were no significant differences between the composition of EOs extracted by HD and MAHD. Both plants showed great radical scavenging activity, with 50% inhibitory concentration values of 0.430 to 0.431 mg/mL for *C. macropodum* and 0.142 to 0.146 mg/mL for *O. decumbens*. Evaluation of minimum inhibitory concentration and minimum fungicidal concentration values showed that the *O. decumbens* EOs were very active against all the tested fungi, which can be attributed to the high amounts of oxygenated terpenes in the EO content. Therefore, MAHD as a fast extraction

technique did not have any adverse effects on chemical composition and radical scavenging activity of *C. macropodum* and *O. decumbens* ⁴¹.

Alternative study compared the relative capabilities of two different extraction techniques, namely HD, and MAHD to separate the EO from the aerial parts of *Artemisia sieberi*, in combination with analysis by GC and GC-MS. By means of the HD method, 47 components were identified in the aerial parts oils, representing 98.6 % of the total composition, whereas by the MAHD method, 30 components were identified, constituting 99.7 % of the oil. The main fundamentals of the HD method were camphor (22.0 %), 1,8-cineole (19.3 %), cis-davanone (15.0 %), camphene (4.6 %) and terpinene-4-ol (3.2 %), whereas the profile of the oil isolated by the MAHD technique was characterized by cis-davanone (29.8 %), camphor (20.8 %), 1,8-cineole (13.8 %), geranyl acetate (5.7 %) and terpinene-4-ol (3.0 %) as the dominant compounds. It can be concluded that the results are comparable, but the main advantage was the time needed to complete the extraction method using MAHD was much less than HD technique ⁴².

The composition and bioactivity of natural plant extracts strongly depends on the extraction technique employed. *Clinacanthus nutans* Lindau (*C. nutans*) is a well-known medicinal plant in South-East Asia that has been traditionally used for treatment of hepatitis, skin-rashes and snake venom poisoning, and recently has attracted attention for its applications for treatment and prevention of cancer diseases. The extraction of bioactive compounds from *C. nutans* by conventional Soxhlet extraction has been described, but this method shows limitations in terms of selectivity, extraction yield, and toxicity of the solvents employed. In this study, phytochemical compounds were extracted from leaves and stems of *C. nutans* by MAE, pressurized microwave-assisted extraction (PMAE) and Soxhlet method to investigate the best technique in terms of yield, extraction time and recovery of bioactive compounds: phenols, flavonoids, phytosterols and β -sitosterol. The extracted phytochemicals and phenolics were considered by GC/MS and ultra-performance liquid chromatography (UPLC). The results showed that MAE was the best technique to achieve a high yield and a maximal total polyphenol content (11.30 ± 0.39 mg GAE/g DM) and flavonoids content (4.66 ± 0.20 mg GAE/g DM) ⁴³.

MAE seems as the greatest effective procedure for the extraction of phytochemical compounds from *C. nutans* in a short time with a reasonable yield and a good selectivity toward bioactive nutraceutical compounds, with high concentrations of antioxidants, anti-inflammatory and antimicrobial compounds ⁴⁹.

Comparing the EO yields isolated from the aerial parts of *Eryngium bungei* bioss. By MAHD head space solid-phase microextraction (HS-SPME) techniques, were analyzed by means of GC and GC-MS methods. The main components of the water distilled oil were found to be borneol (44.4 %), isobornyl formate (14.7 %), isoborneol (9.2%), 1,8-cineol (9.1 %) and camphor (7.9 %), while the oil extracted by MWHD method was mainly composed of yomogi alcohol (14.3 %), terpinolene (14.2 %), cumyl alcohol (13.6 %), borneol (12.4 %), Z- β -ocimene (10.6 %) and sabinene (6.2 %). Moreover, in the oil gained by HS-SPME, the most abundant detected fractions were borneol (22.1 %), camphor (11.1 %), terpinolene (8.1 %), carvacrol (7.5 %) and yomogi alcohol (5.2 %). Despite of some differences present in the oils compositions, all of them were rich in oxygenated monoterpenes. The outcomes confirm the high potential of MWHD, HS-SPME as advanced, environment compatible and promising instrumentations for reliable and fast analysis of the *E. bungei* volatile oil ⁴².

Luque-Garcia *et al.* proposed a MAE of fat from prefried and fried meat and fish. A drastic reduction in the process time (55 min versus 8 h) was achieved with same reproducibility that may be obtained by the conventional method. Besides, the proposed method has the advantage of recycling around 75-80 per cent of the extractant and it is cleaner when compared with conventional Soxhlet ⁴⁴.

Chemat *et al.*, studied microwave accelerated steam distillation (MASD) of EO from lavender flowers. It was revealed that in steam distillation (SD) and MASD the extraction temperatures were same as the boiling point of water i.e. 100°C at atmospheric pressure. When SD and MASD were compared, the time taken to attain the extraction temperatures and also to get the first essential oil droplet, MASD requires only 5 min when compared with SD which requires almost 30 min. As a result the yield of oil obtained at an extraction time of 10 min in MASD was same as that obtained after 90 min by means of SD, which is one of the advanced methods in the stream of EO extraction. The final yield of EO obtained from lavender flowers was 8.86 % by MASD and 8.75 % by SD ⁴⁵.

Chemat *et al.*, stated that extraction time in microwave assisted procedure was found to decrease with increase in temperature. This decrease could be recognized to the fact that with increase in temperature, the vapour pressure of water present inside the celery seeds increased leading to leaching out and evaporation of volatile oil along with water ⁴⁵.

Lucchesi *et al.* studied solvent-free microwave extraction (SFME) of cardamom EO. The results showed that compared to conventional HD, rupture of glands and plant were more rapid when heated with microwave energy. In case of microwave heating, when the glands were subjected to more severe thermal stresses and localized high pressures, pressure build-up takes place within the glands which results in increased capacity for expansion and leading to cell rupture more rapidly than in conventional extraction. Numerical treatment of the results revealed that the selected parameters i.e. extraction time, irradiation power and moisture content of the seeds have significant effect on the output parameters ³⁷.

Asghari *et al.*, compared MAHD with HD method in the extraction of EO from *Thymus vulgaris* L. The outcomes showed that MAHD has taken only 75 min for extracting EO when compared to 4 h in HD. Similarly, MAHD was higher in terms of saving energy. SEM of thyme leaves undergone HD and MAHD provided evidences that sudden rupture of EO glands takes place in MAHD. The refractive indices, specific gravities and color of EO obtained from thyme aerial parts for both MAHD and HD fall within the ranges quantified by Food Chemical Codex (FCC). GC-MS analysis of the extracted EO shown that the use of microwave energy did not adversely affect the composition of the EO ⁴⁶.

Microwave of secondary metabolites of phenolic and flavonoids compounds

MAE has proven to be a more effective extraction technique than conventional extraction methods (heat reflux and Soxhlet) for the extraction of silymarin from milk thistle seeds (*Silybum marianum*). Significant increase from 52% and 60%, respectively when compared with heat reflux extraction. The study showed that MAE not only shortened the extraction time, but also showed better extraction yields compared with conventional thermal extractions (heat reflux and Soxhlet). Also, on the other hand, the microwave exposure time and power used must be carefully monitored, because MAE offers rapid release of the target

compounds in the surrounding extraction solvent and longer extraction times could increase the degradation of extracted phenolics for prolonged extraction under these extreme conditions. Leading to decreased silymarin content longer exposure to MAE probably due to decomposition⁴⁷. Recovery of antioxidant capacities of *Vernonia amygdalina* leaf extract was studied using MAE method. The optimized extract from MAE was compared to that of Soxhlet extraction technique, the extract from MAE resulted in a higher yield of antioxidant activity with more chemical components from the GC-MS analysis. More so, the identified chemical components from GC-MS analysis confirmed the presence of flavonoids which are responsible for the stronger antioxidant activity of *V. amygdalina* leaf. So, it was suggested that MAE can be applied in the large-scale production of antioxidant in pharmaceutical and food industries⁴⁸.

Flavonoids vary in polarity, so the solvents can be highly polar or less polar. Less polar solvents are used for extraction of flavonoid aglycones and more polar solvents are used for extraction of flavonoid glycosides and anthocyanin. Benzene, chloroform, ether, and ethyl acetate are the common solvents for the extraction of less polar aglycones such as isoflavones, flavanones, dihydroflavonols, flavones, and flavonols which are highly methylated⁴⁹. The more polar flavonoid glycosides such as hydroxylated flavones, flavonols, biflavonyls, aurones, and chalcones are traditionally extracted using acetone, alcohol, or water⁴⁹. For microwave extraction of both polar aglycones and flavonoid glycosides, the solvents commonly used include methanol or ethanol, with different concentrations obtained by dilution with water⁵⁰⁻⁵². Also solvents such as acetone and chloroform are used for MAE⁵³. The variation in the concentration of solvents also affects the flavonoid extraction as observed in the case of microwave extraction of quercetin and rutin using different concentrations of ethanol⁵⁴. Also, a decrease in the flavonoid yields with increase in power has been found to be significant when the extraction period was extended^{37,55}. The yield of flavonoids increased remarkably with the increase of temperature from 90 to 110 °C while above 110 °C, the yield increased only slowly, and the extract was found to be scorched.

Polyphenols, the familiar naturally occurring antioxidants, are the richest secondary metabolites in grape wastes. Investigation of numerous non-conventional extraction methods to classic solid-liquid extraction (SLE) to obtain phenolic compounds from grape seeds and skins. Alessandro *et al.* matched SLE, ultrasound-assisted extraction (UAE), MAE and high pressure and temperature extraction (HPTE) in term of extraction yield and antioxidant power of the extract. Solvent of choice concerning methanol and ethanol was the former, both for skins and seeds. Qualitative analyses were performed using colorimetric and High-performance liquid chromatography (HPLC) methods. The maximum content in total polyphenols, o-diphenols and flavonoids, both for seeds (108.3, 47.0 mgGAE gDW⁻¹, 47.2 mgCE gDW⁻¹) and skins (34.2, 10.1 mgGAE gDW⁻¹, 21.6 mgCE gDW⁻¹) was gained with HPTE working in a Parr reactor. While the highest antiradical power was determined in seeds extracts from MAE (78.6 extract µgDPPH⁻¹). Prolonged extraction times increased the amount of total flavonoid (TF), while progressively decreased the number of flavonoids and the antiradical power⁵⁶.

Celia Rodríguez-Pér *et al.*, 2016 test the efficiency MAE and Pressurized Fluid Extraction (PLE) towards the extraction of phenolic compounds from *Moringa oleifera* leaves. The extraction yield, TF, scavenging method and trolox equivalent antioxidant capacity (TEAC) assay were considered as response

variables while the effects of extraction time, percentage of ethanol, and temperature were also studied⁵⁷. Extraction time of 20 min, 42% ethanol and 158°C were the MAE optimum conditions for achieving extraction yield of 26 ± 2%, EC50 15 ± 2 µg/ml, 16 ± 1 Eq Trolox/100 g dry leaf, 5.2 ± 0.5 mg Eq quercetin/g dry leaf, and 86 ± 4 mg GAE/g dry leaf. Regarding PLE, the optimum conditions that allowed extraction yield of 56 ± 2%, EC50 21 ± 3 µg/ml, 12 ± 2 mmol Eq Trolox/100 g dry leaf, 6.5 ± 0.2 mg Eq quercetin/g dry leaf, and 59 ± 6 mg GAE/g dry leaf were 128°C, 35% of ethanol, and 20 min. PLE enabled the extraction of phenolic compounds with a higher number of hydroxyl-type substituents such as kaempferol diglycoside and its acetyl derivatives and those that are sensitive to high temperatures (glucosinolates or amino acids) while MAE allowed better recoveries of kaempferol, quercetin, and their glucosides derivatives⁵⁷.

A closed-vessel MAE technique was improved firstly for the extraction of polyphenols from raw propolis. The results obtained by means of response surface experimental design methodology showed that the best global response was reached when the extraction temperature was set at 106 °C, the solvent composition close to Ethanol-H₂O 80:20 (v/v), with an extraction time of 15 min. In comparison with other techniques, such as maceration, heat reflux extraction (HRE) and ultrasound-assisted extraction (UAE), the extraction with MAE was improved by shorter extraction time and lower volume of solvent needed. The HPLC analyses of propolis extracts were carried out on a fused-core Ascentis Express C18 column (150 mm × 3.0 mm I.D., 2.7 µm), with a gradient mobile phase composed by 0.1% formic acid in water and acetonitrile. Detection was performed by MS⁵⁸.

The method validation showed that the correlation coefficients were >0.999; the limit of detection was in the range 0.5–0.8 µg/ml for phenolic acids and 1.2–3.0 µg/ml for flavonoids; the recovery range was 95.3–98.1% for phenolic acids and 94.1–101.3% for flavonoids; the intra- and inter-day % values for retention times and peak areas were ≤0.3 and 2.2%, respectively. The quali- and quantitative analysis of polyphenols in Italian samples of raw propolis was performed with the validated method. Total phenolic content acids ranged from 5.0 to 120.8 mg/g and total flavonoids from 2.5 to 168.0 mg/g. The proposed MAE process and HPLC method can be considered consistent tools for the comprehensive multi-component analysis of polyphenols in propolis extracts to be used in apitherapy⁵⁸.

Total phenolic content was extracted from aromatic plants such as *Rosmarinus officinalis* using MAE. Compared with traditional reflux extraction, MAE reduced extraction time, diminished solvent consumption and increased extraction yield of total phenolics⁵⁹. Antioxidant activity of phenolic substances extracted from the peel of *Dimocarpus Longan* using MAE was superior to that using Soxhlet extraction⁶⁸. MAE of curcumin from *Curcuma longa* was optimized using Taguchi L9 orthogonal test. The technique showed better precision and dramatically higher extraction yield with significant reduction in extraction time, when compared to Soxhlet extraction, maceration and stirring extraction¹⁵. A sample preparation method based upon MAE of salidroside and tyrosol from the dried roots of *Rhodiola* was established. HPLC coupled with MAE was validated to achieve the satisfactory precision and recovery and was successfully used to measure salidroside and tyrosol in different *Rhodiola* species⁶¹. An efficient MAE technique was also developed to extract scutellarin from *E. breviscapus* for rapid quantification by HPLC. Under the optimal condition, MAE showed high extraction efficiency⁶².

Quinones

Quinones are a ubiquitous class of compounds found in several natural products including plants, fungi, and bacteria. Most of these naturally occurring quinones are synthesized via the shikimate or polyketide pathways that are absent in animals. Quinones derived from plant secondary metabolites possess some anti-proliferation and anti-metastasis effects in various cancer types both in vitro and in vivo. Black cumin seed undergone different processing times including 90, 180 and 270 s and different microwave powers including were applied for optimizing of the extraction process. After microwave pre-treatments, the oil seeds were extracted with screw press with different rates, and then parameter including extraction efficiency, oxidative stability, peroxide and acidity index, free radical scavenging activity as well as the refractive index of the extracted oil was studied. The results revealed that enhancement in the microwave power and the processing time increased extraction efficiency, acidity index and oil peroxide value, but it decreased the oxidative stability value of the achieved oil⁶².

Phenylpropanoids and coumarins

MAE was engaged to extract a coumarin and other phenylpropanoids from the *Cinnamomum cassia* bark using water as the extraction solvent. The results gained verified that higher extraction temperature and longer extraction time absolutely affected coumarin and cinnamyl alcohol contents, but negatively affected extract contents of cinnamic acid, cinnamaldehyde and 2-hydroxycinnamaldehyde (all $p < 0.05$)⁶³.

The extraction of 2-methoxycinnamaldehyde was depended on both temperature and time. These changes during MAE were assumed by the chemical natures of the compounds with various functional groups. So, the temperature and times significantly affected the extraction efficiencies of a coumarin and five phenylpropanoids from *C. cassia* bark when a water-based MAE method was used. This study provides a novel approach to the preparation of the water extract of *C. cassia* bark using MAE⁶³.

Kennouche A. *et al.*, 2015 evaluated composition, antimicrobial and antioxidant activity of clove EO. Volatile oils of *Eugenia caryophyllata* were isolated from cloves after cryogrinding by conventional HD and MAE. The results display that the MAE establishes the acceptable technique for the extraction operations for the yields and the high content in major component and allows minimizing the energy consumption, the heating time and the formation of artefact products. The suggested methods afford more valuable EO with high percentage in eugenol what allows to obtain more biologically active EO. EO from *Eugenia caryophyllata* were exposed to in vitro antibacterial assay alongside human pathogenic *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Staphylococcus carbonarius* using disc diffusion method. The antioxidant properties (2,2-diphenyl-picryl-hydrazyl radical (DPPH)) of EO and pure eugenol isolated were examined⁶⁴.

MAE was also applied to the sample preparation for the determination of chlorogenic acid in *Lonicera japonica*. The nano-liquid chromatography electrospray ionization MS following MAE was proven to be a fast and reliable method for quantitative analysis of chlorogenic acid in *L. japonica*²⁹. Coumarin and melilotic acids in the flowering tops of *Melilotus officinalis* were extracted by MAE. Taking into account extraction yield, extraction time and cost, MAE was considered the best method compared with Soxhlet extraction and UAE⁶⁵. Response surface methodology was used to optimize the parameters for MAE of decursin from the roots of *Angelica gigas*.

Under the optimal condition, the content of decursin in the extract reached 2.52%⁶⁶. MAE coupled with HSCCC was successfully used in the separation and purification of isofraxidin from *Sarcandra glabra*⁶⁷.

CONCLUSION

MAE has some considerable merits such as shorter extraction time, and less solvent consumption compared to conventional extraction methods. The use of MAE for the extraction of phyto-constituents from various plant extracts has shown that it is more suitable for extraction compared to the other methods of extraction. It was regarded as a robust alternative to traditional extraction techniques.

MAE can prove as a boon to herbal product research, if applied to research in discovery of new and effective compounds from plants. There are few studies for application of MAE to herbal drug research. Hence, there is a need to boost the acceptance and value of this novel extraction technique for its applications in herbal drug industry.

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