DOI: 10.1002/slct.201600075

Sustainable Chemistry

Industrial Feasibility of Natural Products Extraction with Microwave Technology

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The industrial extraction of natural products based on microwave irradiation of plant material and volumetric heating is now an industrial reality. Besides significant reduction in waste generation, manufacturing biomass extracts via microwave-assisted extraction (MAE) leads to such technical, economic, and environmental benefits whose entity, we argue, will end the distillation era of solid-liquid extraction using hydrocarbon solvents.

Introduction

Valorisation of agricultural and food residues via green chemistry technologies is among the most important objectives of contemporary chemical research.[1] The environment benefits thanks to reduced waste production, and reduced energy demand; the economy grows thanks to the significant economic value of many bioproducts, new revenues made available to farmers, and jobs creation.

The manufacturing unit of the biomass-based economy is the biorefinery, namely a chemical plant producing chemicals, fuels, and polymers from renewable raw materials. Tens of such biorefineries successfully operate in Europe, particularly in France;[2] even though the factual implementation of such biorefineries has been slowed down by a perceived high risk of adoption of new technologies.[3]

There are many examples of valued products obtainable from food and agricultural residues whose high cost, due to the low materials efficiency of conventional extraction processes producing large streams of contaminated effluents, has so far limited large-scale extraction and utilization. One example is lycopene, a powerful natural antioxidant abundant in tomatoes and other red fruits, with many new applications as nutritional supplement, natural red color for food and beverage, and active ingredient in cosmetic products.[4]

Another example is pectin, a valued natural hydrocolloid obtained from citrus peel, a by-product of the citrus industry, whose cumbersome acid hydrolytic process to isolate it on industrial scale is perhaps one of the most revealing examples of the obsolescence of industrial extraction processes.[5] The process indeed generates such large amounts of acid wastewater, that the high cost to comply with disposal costs enforced in the US in the early 1990s, forced manufacturers (one in California and the other in Florida) to relocate pectin production plants in Mexico.[6]

As put it by Pfennig and co-workers, "plant extraction is a mature technology, where most of the procedures and equipment used today were developed almost hundred years ago".[7] Such process obsolescence sharply contrasts the wide and rapidly increasing consumer demand of natural ingredients in cosmetic, food and pharmaceutical products. Green, industrial extraction methods are among the key chemical technologies of the emerging biorefinery,[8] to bring non-denatured and biodegradable extracts without contaminants to a large number of consumers.[9]

Amongst said new techniques for improving extraction of plant secondary metabolites, intensified extraction relying on microwave dielectric heating and supercritical fluid extraction (SFE) have emerged as some of the most promising alternative techniques for the selective extraction of specific components from plants, flowers and seeds (the other green techniques being ultrasound, instantaneous pressure drop, and pressing).[10] Lately the first important contributions about industrialisation of MAE technology have appeared in the literature, including applications to extraction of boldo leaves,[11] and essential oil from aromatic herbs.[12] From these studies, the striking advantages when comparing MAE to conventional hydrodistillation (HD) are immediately evident. For example, the energy required to extract one gram of essential oil from rosemary is 0.25 kWh for MAE and 4.5 kWh for HD. Yet, while the HD extraction takes 4 hours, in the case of MAE the extraction is complete in 30 minutes.[12]

This study further investigates the economic feasibility of MAE, applied to representative by-products of agriculture producing further evidence that can assist in the transition of the natural products industry from distillation to green extraction technology.

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Unique features of MAE

Microwave irradiation was first used for the extraction of plant secondary metabolites in Hungary in 1986.[13] Since then, extensive researches carried out across the world (Figure 1) have clearly demonstrated the value of the technique for the recovery of value-added compounds such as fragrances, aromas, antioxidants, and pigments from several types of raw materials, particularly of solvent free MAE.[14]

Paré in Canada in the 1990s,[15] followed by Chemat and Cravotto in Europe in the 2000s first decade, have given critical contributions to advance the field from laboratory scale up to the first industrial applications currently unfolding.[16]

Opposite to traditional methods, such as solid-liquid extraction with external heating, in MAE processes heat and mass gradients work in the same direction (from inside outwards), with quicker heating occurring inside the solids where the dissolution of the extract components takes place.

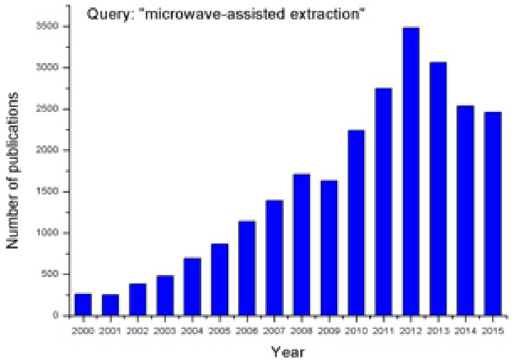

Figure 1. Number of publications in microwave-assisted extraction (1986-2015).
[Authors' graph of data from Google Scholar, 2016].

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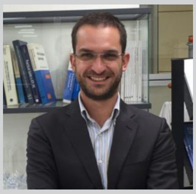

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MAE indeed is based on the localized, dielectric heating of moisture present in all natural materials, especially in vegetal material. Microwaves generated by a magnetron typically at a frequency of 2450 MHz interact with water (and other polar) molecules causing their heating as the molecular dipoles try to orient themselves in the direction of the electromagnetic field. Part of electromagnetic radiation is thus converted into molecular motion, and dissipated as heat. Heating is volumetric: the whole sample is heated at the same time, with heating from inside the biological matrix causing desorption of target compound from into the solvent.[17]

In general, MAE affords much shorter extraction time (from several seconds to 1 h), higher extraction yield, and much (5-to-10 fold) less solvent consumption compared to conventional extraction methods.[17] Furthermore, MAE allows the unique possibility to carry out the integrated extraction of multiple valued substances from a *single* matrix, which is particularly advantageous in the case of readily available agriculture by-products such as waste orange peel. In 2008, indeed, Clark and co-workers in the UK were the first to propose the use of MAE for the future citrus-based biorefinery.[18]

In the same year, Chemat and co-workers described the first microwave-assisted hydrodiffusion and gravity (MHG) for improving plant extraction.[19] The vegetal material is placed in a vessel inside the MW oven, without adding water or organic solvents. Hydrodiffusion and gravity extraction occur due to release of internal water of the matrix. Essential oils and other valued solid components are recovered from the bottom of the reactor via condensation of the distillate.

A biorefinery based on orange peels waste, this time based on integrated green and solvent free extraction processes to obtain essential oil, polyphenols and pectin, was lately described by the same team.[20] Extraction uses ultrasounds and microwaves as the only energy sources without adding any solvent but only *in situ* water from the peels, which was recycled and used as solvent for subsequent extraction of polyphenols and pectin. The combination of ultrasound, microwave, and the citrus peels water allows to obtain high added values compounds in shorter time using only resources provided by the plant which makes the whole closed-loop process intrinsically sustainable with minimal demand of energy.[20]

From lab scale to industrial extraction

In general, microwaves are now widely employed in synthetic organic chemistry for process activation and intensification.[21] Like SFE, however, doubts about MAE often arise when it gets to industrial applicability. High initial investment costs, maintenance and even safety aspects are invoked to justify the natural product industry's reliance on the *status quo* (extraction with hydrocarbon solvents).

Reviewing the field in 2011, Pfenning and co-workers in Belgium were concluding that "the technical complexity of applying microwaves in large-scale equipment is high",[7] making economic transfer to the manufacturing scale questionable. Yang and co-workers in China in the same year reached analogous conclusions, noting that there were few publications on the use of MAE in the large-scale industrial processing of plant secondary metabolites; thus "requiring special efforts to solve technical problems such as the development of microwave-based extractors in order to facilitate the application of microwave assisted extraction to food and drug industries".[22]

Dramatic technical progress, though, occurred in the last five years with developments ranging from the conceptual to the industrial stage.[23] Eventually, the first industrial MW extractors reached the marketplace and were installed at industrial sites, showing that the scale up of microwave-based extraction process to industrial scale is indeed possible and economically attractive.[24]

The main factors to be considered while scaling up are the sample thickness and the frequency of electromagnetic radiation. To allow penetration of electromagnetic waves at a greater depth, large-scale extraction might use a lower frequency (0.915 GHz), with the disadvantage of slower and irregular heating of the sample.

A better solution, thus, is to use a higher frequency (2.45 GHz), but taking into account that the sample should be comprised of parts of 2 cm maximum thickness (because the waves at this frequency have a smaller length and the ability to penetrate the sample). Manufacturers of microwave assisted large scale instruments optimized the chamber geometry, electrical components, and connections to solve the hurdles posed by scale-up. The resulting multimode extractors allow to control the most important parameters affecting the MAE process.

The outcome is reproducible extraction, which is a critical aspect in the commercial production of a consistent natural product (besides the identification of starting raw material) as it allows to standardize the process, and thus the final product.[25] Rotation of the drum in the pilot-scale extractor in Figure 2, for example, ensures a homogeneous microwave distribution through the botanical matrix. Vapor and liquid easily cross the perforated drum circumference.

Cost of manufacturing

Given the higher cost of one such typical extractor when compared to the low cost of conventional solvent-liquid extractors, investors could wonder why to switch to microwave extraction technology. The answer, is simple and twofold: higher quality of the bioproducts, and lower cost of manufacturing.

Assessing the cost of manufacturing of supercritical fluid extraction (SFE) technology using CO_2 first for the decaffeination of green coffee beans and ever since for several types of raw materials, Pereira has recently emphasized that although the initial investment of a SFE plant is high, its operational costs are lower than of traditional extraction plants and therefore it is possible to redeem the extra cost shortly.

"This type of preconception is common to all new technologies, including ultrasound- and microwave-assisted extraction and pressurized liquid extraction, since the investment cost of traditional technologies, namely low pressure solvent extraction and steam distillation, is low".[26]

Pereira's team in Brazil went further by estimating the manufacturing cost of extracts by SFE and different techniques, in-

Figure 2. The MAC-75 pilot scale extractor contains four magnetrons (4 × 1500 W, 2450 MHz). The 150 L stainless steel microwave cavity contains a removable PTFE drum that allows up to 75 L of plant material to be loaded. The system automatically adjusts the power delivered if MW absorption, controlled by sensors, is too low. [Photograph of Milestone srl].

cluding ultrasound-assisted extraction and pressurized liquid extraction, comparing them to classical extraction methods. The supercritical technology invariably leads to production of extracts from natural products at a lower cost than using conventional separation techniques.

By the same token, Manz' team in Spain recently showed that MAE is indeed an economically and technically advantageous technique for the extraction of bioactive polysaccharides mainly from food matrices or food by-products.[27] The comparison in terms of speed, yield, energy consumption of MAE with other conventional (solid-liquid extraction) or emerging techniques (pressurized liquid extraction, ultrasound-assisted extraction), and the simulated scale-up of MAE technique shows that microwaves provide tangible benefits that will shortly be exploited on industrial scale.

In general, the cost of manufacturing (COM) of natural extracts can be determined as the sum of the direct manufacturing cost (DMC) or prime cost, the fixed manufacturing cost (FMC), and general expenses (GE), as in Eq.1.

$$\mathrm{COM} = \mathrm{DMC} + \mathrm{FMC} + \mathrm{GE} \tag{1}$$

The DMC is composed of five main costs: fixed capital of investment (FCI), cost of raw material (CRM), cost of operational labor (COL), utilities (CUT) and waste treatment (CWT). Using the methodology of Turton, the DMC would be given by Eq. (2):[28]

$$\mathrm{DMC} = 0.28\ \mathrm{FCI} + 2.37\ \mathrm{COL} + 1.23\,(\mathrm{CUT} + \mathrm{CWT} + \mathrm{CRM}) \tag{2}$$

The fixed (indirect) cost (FMC) are related to depreciation, taxes and insurance. General expenses (GE) are those needed to keep the organization running and include salaries, marketing, research and development and similar costs not directly associated with the manufacturing process.

A quick evaluation, for example for the extraction of waste orange peel using ten MAC-75 multimode microwave extractors in parallel, is simple. In the case of waste orange peel, available at no cost, the cost of raw material (CRW) in Eq.2 is zero.

In the same equation, the cost of waste treatment (CWT) is also zero, because by-product water containing traces of limonene and sugars can be directly used for irrigation, whereas the solid cellulosic residue can be used as adsorbent material.

To calculate the cost of utilities (CUT) it is enough to consider that each waste citrus peel extraction cycle lasts 1 h, with a power absorption for each MAC-75 of 12 kW.[29] In one working day (7 hours), thus, our plant would consume 840 kWh, yielding about 55 kg of pectin and half liter limonene, both of the highest quality. Typically in Italy one kWh is priced by utilities at 0.20 EUR, translating into a daily cost of electricity of 168 EUR.

As of January 2016, one global chemicals supplier was selling 1 kg of pure pectin from citrus peel (galacturonic acid $\geq$74 %) at 346.5 EUR[30] and 500 mL of *d*-limonene (97 %) at 75.9 EUR. In one day, thus, our small biorefinery would create the equivalent of 19,100 EUR of new economic value.

This simple, yet informative analysis of the effects of the process variables on the COM components shows that, besides the cost of fixed capital of investment, the largest influence on the final manufacturing costs, is the cost of electricity, followed by the cost of operational labor which, nonetheless, can be limited to two persons whose tasks would limit to collect the product at the end of each extraction cycle, and make each extractor ready for the next run.

The green shift in the natural products industry and market

Natural products, namely the chemistry of organic compounds occurring in Nature, is an eminent domain of chemical research,[31] and a central part of chemical industry.[32] Natural products, for instance, continue to be the source of some of the most useful drugs commercialized worldwide. Over the 25 years time frame from 1981 to 2006, of the 974 small molecule new chemical entities, 63 % were other than synthetic, and all the others actually being either natural products or directly derived therefrom.[33]

Besides pharmaceuticals, after one century dominated by synthetic chemicals generally derived from oil, natural products are playing again a critical role in cosmetics, personal care, food and beverage industries. Only in the field of personal care market (skin care, hair care, lotions, soaps, moisturizers, and make-up) the global market will grow at $>$9 % annual rate in the five years between 2015 and 2019.[34] Similarly, with 2014 revenues exceeding $13 billion, the fragrance industry is expected to grow at $>$5 % annual rate until 2019, with revenues estimated above $17 billion by 2017.[35] In both cases, consumers increasingly caring about their health and well-being demand increasing use of natural in place of synthetic products.

Put simply, ever more informed consumers across the world wish to take care of their skin, hair and body using beneficial products, devoid of any toxic effect; and they identify in natural (or organic) products the answer to most of their requirements, even though natural and organic personal care products are generally more expensive than their synthetic counterparts.

As a result, physical and online stores increasingly stock and sell natural and organic personal care and beauty items. Gone are the days in which organic and natural skincare products were a rarity, reserved for the rich and wealthy able to afford them on a regular basis in substitute of ordinary chemical-based face creams and lotions.

In this rapidly changing market landscape, companies extracting natural products critically need new technologies capable to provide extracts of high quality of products at affordable cost. Cosmetic and personal care companies, indeed, will buy safe, certified products (to confirm their authenticity and adherence to industry guidelines) available at affordable price. Natural and organic products need to be free from pesticides, growth hormones, preservatives, and additives (including artificial colors).

It is this new consumer demand that suddenly renders attractive technologies such as SFE and MAE that are, respectively, 45 and 30 years old. Technologies such as extraction with $scCO_2$, that for decades since 1970 had been restricted to affluent coffee manufacturers willing to decaffeinate part of their production, are now routinely used by relatively small and medium size enterprises such as California-based Draco Natural Products to extract all sort of lipophilic natural products; while a pioneering company in Germany using supercritical CO_2 (Nateco2) is currently doubling its extraction capacity to the "booming market of natural supplements".[36]

The huge demand of natural products devoid of contaminant organic solvents, indeed, now suffices to ensure high revenues, and profits, with which to bear the higher initial investment cost of the high-pressure $scCO_2$ technology, affording extracts of exceptional quality at *lower* operational cost than traditional solid-liquid extraction, provided that enough amounts of product are demanded.

This trend is general and extends to all sort of functional products for human consumption. The natural antioxidants market (vitamin C, vitamin E, polyphenols, and carotenoids), once a negligible niche of the overall antioxidants market, is expected to surpass the $ 4 billion threshold by 2022.[37] Again, reputed market analysts ascribe the rising global demand to increased consumer awareness regarding the health benefits of natural antioxidants in both personal care and in functional (fortified) food and beverage products containing natural antioxidants.

This shift in customer demand, which directly translates into economic profitability, has changed the way natural product companies approach the manufacturing process. Indeed, the natural antioxidant market key players, which once comprised companies such as Indena and Naturex in Europe, and Tianjin Jianfeng Natural Products and Ajinomoto OmniChem Natural Specialties in Asia, now includes also long time makers of synthetic antioxidants such as DSM and AkzoNobel.

From a manufacturing viewpoint, all these companies will opt to rely only on clean extraction technologies, creating the long awaited demand for MAE and SFE extraction technologies.

To paraphrase Pereira again,[26] MAE is a technically and economically feasible process to be used at the industrial scale; but since little information about industrial costs is disclosed, generally MAE technology is discarded due to high investment cost.

The technical feasibility and economic attractiveness of microwave-assisted extraction of natural products is indirectly shown by the first successful companies commercializing extracts obtained via MAE. Extracts are used in a wide variety of products including foods, beverages, cosmetics, pharmaceuticals, and health supplements, with some extracts sold for as much as > $10,000 per kilogram.

Founded with the Phytobiotex name in 1998 in France, and then purchased by Croda's Novarom, Crodarom has been amongst the first companies to use microwave processing at industrial scale for the production of plant material extracts.[38] The company today manufactures > 1,000 t per year of active plant extracts for use in personal care and industrial applications at in the Lozere region.

Another company, also based in France, using microwave extraction as a tool for obtaining extracts or active compounds is Oleos,[39] using a purely physical extraction process based on focused microwaves with high power density combined to ultrasonic cavitation at low frequency, to produce > 50 different plant oily extracts combining oil with different functional molecules. No chemical product or organic solvent is used allowing organic certification of the products.

On mid 2014, Canada's Radient opened the largest microwave extraction plant currently in the world in Edmonton, Alberta. The company uses Paré's patented microwave-assisted processing technology[40] to cause instant, pressure-driven extraction of speciality natural compounds (lipids, alkaloids, terpenes, proteins, phenolics and glycosides) from various plant products such as flax, rosemary and vanilla beans to the specifications of its customers in cosmetics, nutrition and pharmaceutical manufacturing.[41] At peak capacity, the new facility, capable to process up to 200 kilograms of biomass per hour, is planned to produce > $20 million of product per year.

Conclusions

In one of the main trends of the emerging bio-economy, consumers across the world increasingly demand safe, natural products for personal care, health, food, well-being and for beauty. This translates into massive demand of botanical extracts (secondary metabolites) obtained through extraction processes radically greener than conventional solid-liquid extraction using hydrocarbon solvents.

Natural products companies that have always relied upon traditional processes are now considering to switch to supercritical fluid extraction and to microwaves. Compared to SFE, MAE is still in its industrial infancy even though it should be highlighted that microwaves are widely applied in the food industry for drying and defrosting processes carried out in huge microwave tunnels.

The operational simplicity of the MAE technology, its unique versatility and the recent availability of MW-based industrial extractors such as that installed in Canada in early 2014, will make the microwave technology economically attractive to the numerous natural product manufacturers who will progressively abandon solid-liquid extraction practices. Eventually, green extraction based on microwaves will translate in one of the most relevant achievement of contemporary chemical research. This study will hopefully accelerate the transition.

Acknowledgements

This article is dedicated to Professor J. R. Jocelyn Paré, New Brunswick Innovation Research Chair in Medical Technologies, for all he has done for the development of microwave-assisted extraction technology. We thank Professors Laura M. Ilharco, University of Lisboa, and Alexandra Fidalgo, Universidade Europeia (Lisboa), for fruitful co-operation in this field of our studies.

Keywords: Microwave-assisted extraction · biorefinery · green extraction · industrial extraction

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Submitted: January 29, 2016
Accepted: March 6, 2016