Choosing the Right Extraction Method

By Steve Myers, Senior Editor

The process of botanical extraction, drawing specific compounds from raw plant material, can be achieved by many methods. The simplest and most-recognizable form, on a small scale, is when hot water is used to make tea or coffee. In this case, water acts as a solvent to separate key compounds from the raw material. Solvent extraction methods using water or chemical solvents are popular in the botanical extract industry. Still, other methods range from older to newer and from simple to complex. Choosing the right extraction method for a given ingredient or product requires consideration of the characteristics of each available method.

“There is no right extraction method, it has to be designed for the product,” said William Meer, Ph.D., director of extract operations for BI Nutraceuticals.

Each method has its own range of compounds it can extract, and comes with specific cost and other considerations. TK from Valensa International explained tinctures extract a wide range of compounds including waxes, lipids, sterols and free fatty acids, but they have less success on steam non-volatiles and high molecular weight compounds. Expeller press methods produce slightly better results on steam volatiles, but are not dependable for extracting carotenoids, long-chain alcohols, sterols and waxes, and are also not good for high molecular weight compounds. Steam distillation has an even narrower compound list, drawing out mostly steam volatiles and essential oils. The two methods targeting the full range of plant compounds are extraction with strong solvents—moderate solvents can extract less than half as many compound types—and high pressure carbon dioxide (CO2) extraction—low pressure pulls out about half as many compound types. Still these two comprehensive extraction methods have challenges.

Chemical solvents can be harsh and toxic. Post-extraction purification is an important step to remove solvents or limit solvent residues present in the final extract. Purification is a continually improving step that should be driven by expertise and research and development (R&D) efforts to limit solvent residues and other impurities.

Regulations often restrict types of solvents used and limit solvent residues for safety reasons. FDA, EFSA (European Food Safety Agency) and TGA (Therapeutic Good Administration, Australia) organize solvents into classes of potential toxicity and impose limits on solvent concentrations in final products made for human consumption.

The American Herbal Products Association (AHPA) offers guidance and other resources that can help companies decide on solvents and acceptable residues. The guidance is based on the current International Conference on Harmonization (ICH) document, “Impurities: Guideline for Residual Solvents,” and outlines Class 2 (inherently toxic) and Class 3 (low toxic potential) solvents, and their respective permissible daily exposures and concentration limits. AHPA’s guidance reminds companies several solvents are listed by the State of California as chemicals known to cause cancer or reproductive toxicity, so their use may result in compliance issues with California Prop 65 requirements.

The U.S. Pharmacopeia (USP) is a popular resource for dietary supplement botanical extract standards that can help establish specifications for identity, purity, strength and composition, as well as limits for contaminants, including solvent residues. "While the selection of the extraction methods is determined by each manufacturer, USP public standards could be used by the buyer and the seller to level the playing field and as common language for comparison of the extracts that are derived by different manufacturing processes," said Nandakumara Sarma, Ph.D., director of dietary supplements at USP.

Sarma noted USP provides both generalized guidelines and specific methods. "For example, limits for impurities and contaminants (pesticides, elemental impurities, microbial load and residual solvents) are covered through several USP General Chapters, which are 'guidances' on how to address several aspects of establishing quality standards," he said. "Appropriate limits for these impurities and contaminants are provided in individual monographs for specific extracts, in addition to orthogonal methods for identification and composition. In addition, USP monographs also define quality expectations for the powdered plant materials that form the source of the extracts."

The American Botanical Council (ABC) also offers an extensive collection of botanical monographs and other resources that can help guide and inform botanical extraction. ABC founder and executive director Mark Blumenthal paired with Jay Pierotti, Ph.D., founder and principal of Botanalytics LLC, to author a book, "Solvents Used in the Manufacture of Botanical Extracts, Food Flavors and Natural Food Ingredients," pending publication by ABC.

Water is a popular solvent, and extracts a wide range of water-soluble and polar plant constituents such as flavonoids. Alcohols such as ethanol and methanol are also effective polar compounds, and are more preservative than water. Due to its chemical structure, methanol can also extract some non-polar constituents. Glycosides are an example of a plant compound soluble in both water and alcohol. In many cases, a mixture of water and alcohol is used as the solvent to maximize the number of compounds extracted from certain botanicals.

Hydrocarbon solvents like acetone, chloroform and hexane are strictly non-polar, so they are adept at extracting non-polar compounds such as lipids and fatty acids. Again, depending upon the compounds to be removed from the botanical material, extraction methods will often involve a mixture of polar and non-polar solvents, an alcohol and a hydrocarbon for instance.

Some of these chemical solvents can be toxic and highly flammable, so they are ideally used only when necessary and when residues can be completely removed from the final extract or satisfactorily limited. Further, each solvent has its own pros and cons relative to availability and cost, which are factors in which extraction method and solvent is chosen for a given product.

"The overriding factor is the ability to process a single product in volume," Meer said, noting BI extracts a multitude of products using a batch operation. "We use a classical extraction method in either small, medium or large stainless steel percolators with solvent recirculation."

Solvents are chosen based on the product and the desired constituents in the finished extract, and BI also provides toll extraction and will adjust solvent requirements to meet customer needs. "Federal laws also limit solvent choices," he reminded, advising residual solvents need to be checked and meet standards. Junius Rahardjo, CEO and co-founder, Javaplant, said customers have the freedom to explore methods and put forth requirements by way of specifications. "Customers often times come to our pilot facility to play around with our extractors and validate their own methods," he said.

Otherwise, they look to Javaplant for guidance on the right extraction methods. “Knowing their requirements and concerns, we then can give some ideas of the solvents to be used and at what configuration (if ethanol-water is the case to be involved),” he explained. He stressed the importance of knowing the solubility levels of the extracts beforehand, which will help determine the temperatures to be set for the extraction process.

Expected bulk density of the finished extracts can be another factor, as it can determine what drying system is to be used—according to Rahardjo, vacuum drying generally makes dried extracts have a higher density than spray drying. However, intended application for the extract is a factor. “Bulk density will not matter that much if the customers intend to apply the extracts to ready-to-drink functional or nutritional beverages,” he explained. “On the other hand, high bulk density is everything for the customers who intends to apply the extract to capsules and tablets.”

Javaplant primarily uses ethanol extraction. “Many customers are accepting extracts with solvent residues as long as it is within USP guidelines,” Rahardjo reported. “On the other hand, a few customers are very strict.” If the solvent-free extraction is a must, then Javaplant can only offer water extraction, which results in limited extracts, mostly crude extracts, not purified ones. “Supercritical CO2 is the only way to do the solvent-free extraction and it is costly to invest in and to run,” he said.

NDI Question

As originally proposed in FDA’s draft guidance on new dietary ingredients (NDIs), use of a solvent to prepare an extract could render a pre-DHSEA (i.e., “grandfathered”) ingredient an NDI requiring notification. This was one of the most contentious points of disagreement between industry and FDA, but it remains to be seen whether the final guidance, which is overdue, will maintain this position on solvent extraction.

Supercritical extraction uses CO2 instead of organic solvents. At a temperature and pressure above its critical point, a molecule will become a supercritical fluid, which is not quite a gas, but not quite a liquid. Supercritical fluids can be used under high pressure to extract a full range of phytochemical types. CO2 has a high diffusion rate that can penetrate the material quickier than liquids. It is a pure substance found in nature and is, thus, easily removed from the final extract without leaving any residue.

Among its advantages, supercritical CO2 extraction has the flexibility to extract specific compounds, and it operates at temperatures lower than expeller press and organic solvent methods. It also involves no oxygen, thus better preserving the extracted compounds.

Solvent-free extracts have drawn more attention in the nutraceutical industry,” noted Lixin Ding, Ph.D., director of R&D for BGG. “Consumers not only want nutrient supplements, but they also care about the safety of what they are taking.”

However, supercritical CO2 extraction is not ideal for all ingredients. Ding said BGG only uses this technology to produce ingredients that are suitable for this technology. “Basically, the technology is applicable to materials that are lipid soluble with low polarity,” he explained, noting this technology will immediately apply to several of the company’s existing ingredient lines.

The other less than ideal factor may be the cost to set up and run supercritical extraction. Due to costs, many companies such as BGG will offer both organic solvent and supercritical methods. “Supercritical-processed products are optional to our customers,” Ding noted. “For each product to which supercritical is applicable, we offer both conventional and supercritical grade so customers can choose what best fits their budget and requirement."

Deciding on the best extraction method for a given product involves many considerations, the first of which is the desired specifications for the final extract. This includes not just the types and concentrations of plant compounds, but it also depends on the desired marketing (e.g., "solvent-free"), target market (local regulations, such as California's Proposition 65) and, as always, costs. Knowing the pros and cons of the various available extraction methods and utilizing key resources (e.g., USP, AHPA, ABC, etc.) will help narrow down the decision. In the end, the best ally may be the extraction partner, as any high-quality extract supplier should have extensive extraction knowledge and expertise.