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Supercritical Fluid Extraction Of Nutraceutical Products

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Carbon dioxide is non-toxic, non-flammable, odorless, tasteless, inert, and inexpensive. The critical temperature of carbon dioxide is 88°F, just above room temperatures. In the past five years research and process development activity has focused on utilizing supercritical carbon dioxide technology in processing fine chemicals, pharmaceutical intermediates, and nutraceuticals. In addition to being a solvent for extraction and fractionation (purification) of organic compounds, carbon dioxide is increasingly being utilized as a medium for reactions, as a micronizing agent in Rapid Expansion in a Supercritical Solution process (RESS), as an anti-solvent for crystallization in Gas Anti-Solvent process (GAS), and as a carrier solvent for coating and depositing materials onto or into a solid matrix. Carbon dioxide technology is one of the fastest growing new process technologies being adopted by the food, pharmaceutical and nutraceutical industries.

Supercritical fluid technology will allow nutraceutical companies to develop products of standardized concentration of active ingredients, and will simultaneously produce nutraceutical products of much higher concentration (higher yields and purity) and quality (with less creation of artifacts), than possible by conventional chemical engineering unit operations, such as liquid/liquid extraction, distillation, mechanical micronization, liquid and/or gas phase reactions, etc.

Advantages of Carbon Dioxide as an Extraction Solvent for Nutraceuticals

Carbon dioxide as a solvent has many advantages. Probably the most important advantage is that it is a GRAS solvent that leaves no traces in the product. After extraction, the carbon dioxide is recycled and any trace carbon dioxide in the product dissipates to the atmosphere within a few hours. Also, unlike solvent extraction, the carbon dioxide is readily recycled by pressure and temperature adjustment, which is very mild and does not harm the product. Another advantage of supercritical fluid extraction is the capability of fractionating products to create co-products. Solvent extraction requires a distillation step, (in which top notes are lost and distillation notes are created), that many times alters the taste, aroma and chemical composition of the product. Also, trace quantities of residual organic solvent are usually present in the product.

Botanicals can be fractionated to produce a natural color fraction, an aroma fraction, an anti-oxidant fraction and/or a flavor fraction. This is important in producing nutraceuticals because unwanted strong flavors in certain botanicals such as garlic and rosemary can be separated from the nutraceutical components.

Finally, supercritical fluids can be adjusted to selectively extract certain compounds. For example, the supercritical fluid solvent can be adjusted to extract the pesticides from ginseng. The supercritical fluid process can be further adjusted to extract allergenic compounds from the gingko biloba. Supercritical carbon dioxide is finding broad acceptance in the nutraceutical industry because it does not harm products and produces higher concentration (quality) extracts.

Production Scale SFC

Production scale SFC has been successfully used for the separation of enantiomers and fatty acid esters. Large quantities of DHA and EPA ethyl esters from fish oils are routinely separated to >95% purity on a commercial production scale SFC unit.

Extraction of Fermentation Broths

Supercritical carbon dioxide countercurrent column extraction is currently being investigated as a new process for the extraction of bioactive compounds from fermentation broths. This process offers an inexpensive method to extract and simultaneously fractionate compounds of interest without leaving organic solvent residues in the product.

Partial List of Nutraceutical Products that can be Processed by Supercritical C02

- Extracts of chamomile flowers for anti-inflammatory and anti-spasmodic bioactive compounds (e.g. sesquiterpene, lactone, matricin, etc.)
- Extract of calamus root as an appetite stimulant—higher yield with SFE (8.3%) when compared to steam distillation (6.4%)
- Extracts of turmeric for bile preparations—no artifacts such as tolylmethylcarbinol created in steam distillation
- Valarian as a sedative preparation—valepotriates obtained undecompossed and at high yield (>90%)
- Wormwood extract as a carminative, cholagogue and stomachic—removal of toxic βthujone by fractional extraction from thermally unstable pharmacology active components
- Hydrogenation reactions in supercritical carbon dioxide that are a factor of 1,000 faster than conventional hydrogenation reactions with greater control over *trans* isomer formation
- Extraction of fermentation broths producing vitamins with bioactive compounds
- Enzymatic reactions in supercritical fluids such as conversion of lipids to methyl or ethyl esters
- Saw Palmetto—higher concentration of phytosterols (active ingredients)
- Ginseng—extraction of pesticides without extracting significant quantities of active ingredients

- Echinacea—more concentrated extract obtained by SFE than conventional technologies
- Feverfew—more concentrated extract obtained by SFE than conventional technologies
- Chitin (glucosamine)—able to separate astaxanthin co-product from chitosan using SFE, able to demineralize shells, and other processing steps
- St. John's Wort—more concentrated extract obtained by SFE than conventional technologies
- Kava-kava—more concentrated extract obtained by SFE than conventional technologies
- Gingko biloba—SFE reduces allergenic compounds in extract
- Garlic (allicin)—SFE extract more concentrated and deodorized plus higher yields when compared to conventional technologies
- Evening Primrose oil—more concentrated extract obtained by SFE than conventional technologies
- Rosemary extract—SFE extract more concentrated and deodorized plus higher yields when compared to conventional technologies
- Grape seed extract—more concentrated extract obtained by SFE than conventional technologies

References

Kim, J-Hl, Paxton, E. R., Tomasko, D. L. Microencapsulation of Naproxen Using Rapid Expansion of Supercritical Solutions. *Biotechnology Progress*, Vol.12, No. 5;1996.

Subramaniam, B., Rajewski, R. A., and Snavely, K. Pharmaceutical Processing with Supercritical Carbon Dioxide. *J. Pharmaceutical Sciences* **86**, No. 8. 1997

Poudrier, J. K. SFC Boosts Drug Discovery and Other Processes. *Today's Chemist at Work*. January 1998.