Advances in Applying Critical Fluid Technology and Some Inconvenient Truths

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ABSTRACT

The content of this plenary lecture is divided into two sectors: pertinent advances in critical fluid technology (CFT) and the adoption or integration of the CFT platform for industrial processes to produce commercial products. Results will be presented from the University of Arkansas and the consulting-educational activities of CFS. Current trends in supercritical fluids which will be discussed are:

- Advantages attendant to using higher processing pressures
- The use of subcritical fluids ($T_r < 1.0$) including LCO_2, DME, H_2O etc.
- Pretreatment processing on substrates prior to and utilizing critical fluids
- Advances in using critical fluids applied to processing aqueous-based media
- Problems in implementing multi-unit operations using CFT at industrial scale

Specific subjects that will be discussed regarding the above are treatment of biomass, algae, and recovery of chemicals from dilute aqueous systems. Fluid utilization under their T_c under mild compression, and their attendant advantages, as applied to solute recovery from aqueous systems will be illustrated with examples. The use of high processing pressures (>700 bar) in terms of enhanced targeted solute recovery and prophylactic benefits on the extract will be documented for high value-antioxidants and products whose stability is enhanced by exposure to CFs

The second part of this lecture is devoted to the success or failure in commercializing and/or producing saleable products from sub- and super-critical technology. The featured topics are as follows:

- Over 96% of academic/institutional research in CFT is a commercial failure – Why?
- Failures are particularly significant in the areas of reactions, particle formation, etc.
- What are the barriers and difficulties in avoiding the “Valley of Death” in CFT
- Newer products and processes developed using CFT – successful scenarios
- Future needs in CF processing – with an emphasis on continuous/integrated systems

With regard to the above, the development and issues regarding GMP-compliant CFT processes are limiting implementation in certain cases. There is a need for continuous solids feed systems for contacting CFs with neat solids and aqueous slurry feeds. Aqueous-based processing must embrace conditions below and above the T_c of water including higher operating pressures that are consistent with sterilization of the end product (ex. ‐ PATS ‐ pressure-assisted thermal sterilization). New products proudly stating the application of the “supercritical” medium continue to evolve with additional applications such as extraction of cannabis, laundering of banknotes, and marine/algae-derived products. The lecture will con clude with a realistic assessment of the potential integration of the CFT platform into re- ne able fuels transformation including various bio-refinery schemes.

INTRODUCTION

In this plenary lecture, advances in the application and commercialization of sub- and super-critical fluids - the resultant processes and products – will be described. This is based on the author's consultation, review, and assistance in implementing over 550 CFT projects since 1970, including over 20 in the past two years. Also evaluated are both examples of processes and products that have not been successful and the reasons for their failure. It behoves the technologists in CFT to have an understanding of the commercialization process to avoid the "Valley of Death" that lies between developments in academic and government laboratories and "success" – as defined by realizing an economically-sustainable process and making a saleable product. The latter is a harsh definition of the application of CFT success, since it does not include simply institution technology transfer – only economic - not intellectual success. What follows are examples of success and failure in applying the CFT platform which are focussed mainly in the fields of food- nutraceutical-bioactives processing, cleaning using CFs, cosmetics development, fuel production, and some materials processing in which the author has had some experience.

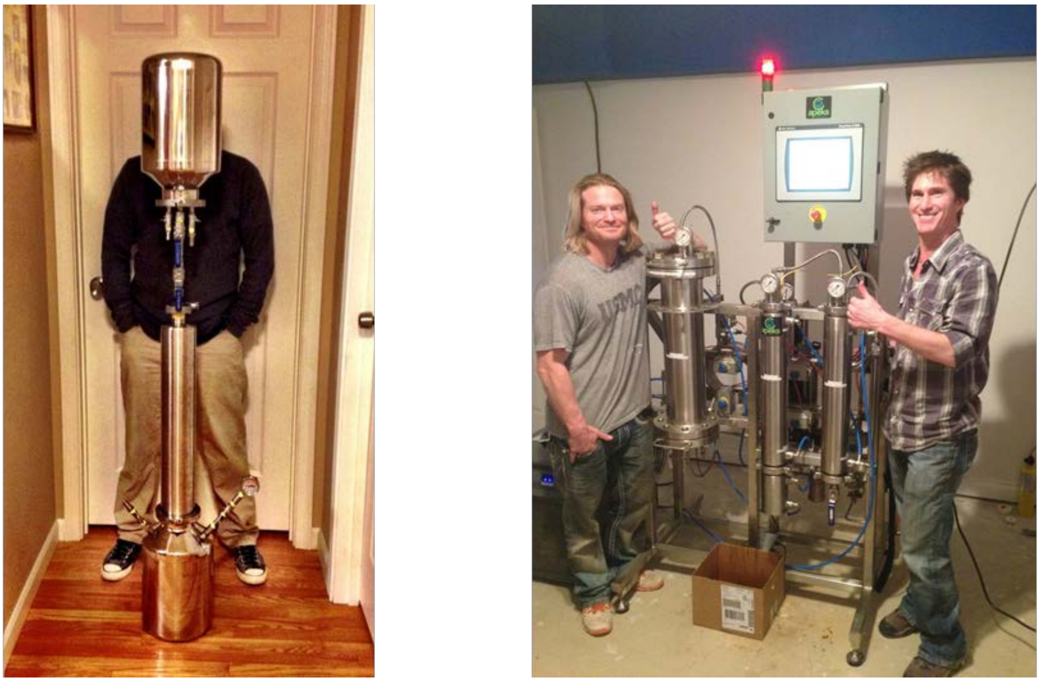
A number of new and excellent reviews and books have recently appeared which document advances in applying CFT [1-20]. We discuss here only a few examples due to space and time limitations that are in the author's area of expertise and experience. However, they are typical of not only advancements in applying the CFT platform, but also of some of the issues involved in overcoming barriers to the adoption of CFs as a processing option and creating products from them.

ADVANCES IN APPLYING CRITICAL FLUID TECHNOLOGY

The legalization of cannabis (marijuana) in multiple states in the USA has increased the visibility of SC-CO_2 as a consumer friendly production method. This is in stark contrast to the use of propane or butane to extract "honey oil" from the cannabis plant and its inherent dangers. Shown in Figure 1a is a home-built "honey oil" extractor in which the 2.5 L column holds 2 lbs. of compacted cannabis seed. A 10 L butane feed tank provides a 4:1 solvent to feed ratio for a nearly complete extraction in a one-pass system. Such units can be bought on E-Bay starting at ~$5,000. However the inherent danger in using such systems in the hands of inexperienced and non-technically trained operators (explosions have occurred) is giving way in the USA to the use of sub- or super-critical fluid extraction with CO_2 at low pressures. Over 40 such CO_2 units, largely made by Apeks Supercritical company (Figure 1b), are in use primarily in the USA.

Another area of intense activity is in the CF-based processing of marine or algae-derived products. Examples of marine and algae-derived products that have been processed using critical fluids include the following:

Fish Derived Oils
Seaweed
Krill
Algae – Derived Oils and Antioxidants
Green-Lipped Mussel
Compounds from Coral
Stem Cells from Sea Turtles
Processing Wastes



(a) (b)

Figure 1: Cannabis extractors: (a) butane-based, (b) carbon dioxide - based

Some marine or algae derived CF extracts consist of multi-functional components designed to enhance such properties as antioxidant efficacy via synergism between the components. An example would be a krill SF-derived extract composed of the bioactive components of omega fatty acids, natural pigments (i.e. astaxanthin), and phospholipid (PL) moieties. This has given rise to ultrahigh pressure SFE conducted at CO_2 pressures between 70 -100 MPa, or higher. The theoretical basis of this approach has been rationalized by King in terms of an extended solubility parameter theory [6] which allows estimates to be made of solute solubility maxima in CFs based on solute molecular structure. Using this approach, solubility maxima for PL-type solutes occur at pressures above 73 MPa for non-polar PLs and even higher pressures for polar PLs. Polar-lipid extractions can also be conveniently processed using dimethyl ether (DME) at 40^{o}C at much lower pressures as demonstrated by Catchpole et al [21].

Estimates for the omega-3-fatty acid market are $13 billion annually (2011) as reported by GOED, a worldwide consortium of omega fish oil-derived products. Within the USA, the omega fish oil health supplements represent 10% (3rd highest) of the top ten dietary supplements taken by US adults more than 20 years old, with a 11.6% growth rate/yr. [22]. The nutritional lipid market place is $3 billion for 2013 – phytosterols as a sub-class commanded 195 million in 2013. It has been demonstrated the CF technology is amenable for processing the various forms of omega-3 fatty acids – including triglycerides, free fatty acids, esterified acids, as well as the omega 3-moiety incorporated in other types of lipids, such as phospho- and glycol-lipids. This has given rise to novel folding techniques involving inverse SFE to remove unwanted lipid matter to obtain clinical levels of natural oxidants. Such techniques are often combined with more traditional methods of extracting natural oils which can include solvent extraction or expelling.

Similarly, the cosmeceutical market has seen an increase in critical fluid derived products – a significant change from their limited use and availability over two decades ago. This in part reflects a change in formulation strategy within that industry which was very tradition bound with respect to ingredients; similar considerations hold in the field of fragrance chemistry. It is now recognized that CF-derived materials are in many ways superior and can improve the various product lines which include jojoba oil, squalane, wax esters, polycosonols, etc. These chemicals have been formulated into skin whiteners, natural antioxidants (astaxanthin), and a multitude of elegant products as offered by Joben Biomedical in Taiwan.
Integration of CF processing particularly in the area of renewable fuels and co-products has taken several forms when applied to bioethanol, biodiesel biobutanol, liquefaction or pyrolysis, and gasification. These processing modes include:

- SC-CO_2 for SFE and fractionation
- Subcritical water extraction (SWE)
- Sub- and supercritical methanol for biodiesel
- Subcritical water for biomass pretreatment and hydrolysis
- Subcritical water for liquefaction
- Supercritical water for gasification

Subcritical water-based extraction processes have largely developed from their initial use as an alternative solvent media in analytical applications and their development has been considerable influenced by pressure liquid extraction (PLE) modules such as the ASE^{TM} system available from the Dionex Corporation. These modules are useful for rapidly screening possible extraction applications and their optimization; however they do not completely address the problems associated with the scale up of a SWE process. To make SWE applicable on a larger scale requires the development of (1) continuous feed systems, (2) inexpensive batch extractors, and (3) appreciation of the relationship of residence time in the extractor with respect to both extraction and reaction kinetics. Our experiences in developing alternative methods to replace hydroethanolic extraction as applied to grape and berry pomaces has embraced some well-known concepts such as hot water espresso extraction, a "supercritical" Charmat approach, a hot-cold method [11], and most recently integrating SWE with an expeller.
Subcritical water for biomass pretreatment and subsequent hydrolysis is acknowledged [23] as a method for the production of sugar monomers from cellulose-hemicellulose-lignin containing biomass, but its effectiveness is highly dependent on the recalcitrance of the target biomass substrate. However it competes with several other reactive pretreatment options although its capitalization costs are competitive with these other options. It has also been demonstrated by various research groups that carbonated water can provide an auto-catalytic effect in depolymerizing naturally-occurring carbohydrate polymers [18,24] as it has in other reactions in the presence of CO_2 and in the Clean Tan CO_2- assisted dyeing process.
Difficulties have existed in implementing certain areas of CFT such as the promising rapid supercritical methanol (SC-MeOH) esterification-transesterification process, and its coupled option with subcritical water hydrolysis (Saka-Dana process). The primary barrier to implementing this process is the concern for safety due to the high temperatures involved. Despite these concerns pilot plant units have been implemented in Japan, and the recent announcement of the Jatro Super^{TM} process being implemented in the USA is encouraging.
Slowly the processing industries that utilize CFT have begun embraced multiple fluid platforms because of: (1) customer demand, (2) more effective utilization of their pressurized

equipment and facilities, and (3) and the ability to "green" an entire extraction process. Multi-fluid processing equipment and plants are now becoming available as demonstrated by Separex, Applied Separations, and other firms for the integration of SC-CO_2 with subcritical water processing. Such processes continue to evolve since the suggestion of the multi-fluid processing possibility by King in 2003 [25]; the hybrid process described by Goto et al. [26] is a derivative of the original concept. The coupled fluid process opens the possibility of multi-unit processing of bio-renewable feed streams which augment extraction using CFs with reaction chemistry utilizing CFs – hence integration into a biorefinery. Several commercial companies are now employing duo extraction media to produce bioactive extracts from natural products, e.g. Draco Natural Products.

FAILURES IN CFT TECHNOLOGY

There is unfortunately a very high rate of failure in certain areas of CFT. These are as follows:

- Reactions in critical fluid media
- Particle technology using CFs, particularly in the pharmaceutical industry, etc.
- Certain areas of polymer technology
- "Cleaning" with CFs – a mixture of success and failure
- Bio-renewable fuels due to competitive processing technologies
- Recovery and purification of chemicals from aqueous media

As an example of disappointment in CFT, consider the area of reaction chemistry. In the areas of polymerization, chemical intermediates manufacture, hydrogenation, and enzymatic-initiated reactions in the presence of CFs, there are few if any of these reaction modes that have been carried to successful commercialization. This includes the shutting down of plants or abandonment of plans to commercialize a process. Some of these proposed academic concepts were naïve to start with, such as the position to produce biodiesel via enzymatic-initiated esterification. Aside from cost, the sheer product throughput/time requirements make this approach unattainable.

Another issue that one must deal with in the commercialization of CFT is if the process is amenable for integration with existing plant processes. This becomes a critical factor when one is considering using CF-based process with a feedstock that has potentially toxic components. Examples of this include the "Super Rubber" approach for treating used car tires and the author's saga in the SFE of cedarwood oil. Integrating these promising technologies into existing CF plants producing foodstuffs, nutraceuticals etc. meets with considerable resistance.

PROBLEMS IN APPLYING CRITICAL FLUID TECHNOLOGY

What are some of factors that terminate the CFT "pipeline"? Listed below are some of the problem areas that seem to dome the development of CFT:

- A lingering perception that all CFT-based processes are expensive to implement
- CFT unit processes are largely batch-based; there is a need for reliable continuous feed systems for both CO_2- and water- based processing

- The multi-use of processing equipment where a toxic principle is involved
- Application to large volume throughput processing
- Short term interest in CFT by industry
- Lack of genuine GMP processing capabilities in certain areas of the world
- Lack of interest in producing low cost equipment for small processors

Perhaps the most vexing question asked by industry and investors is "why use CFT at all"? It behoves one to consider the existing industrial process or culture one is trying to replace with CFT. Examples of fool hardy attempts to implement CFT in a number of industrial settings exist, among these large production volume applications, such as the Unicarb coating process and the biorenewable fuels industry. An interesting situation occurs in the production of algae for biorenewable fuel where SFE has been considered as an extraction option. If one considers Sapphire Energy (USA) as a prototype large volume algae oil producer (~10,000 barrels/day) than it is unlikely that SFE is viable method to process their algae oil which is transformed to fuel via hydrothermal liquefaction. However other producers of algae oil are using SFE with CO_2 with a focus on the nutritional health food market – thus one must consider the targeted commercial end use in incorporating CFT.

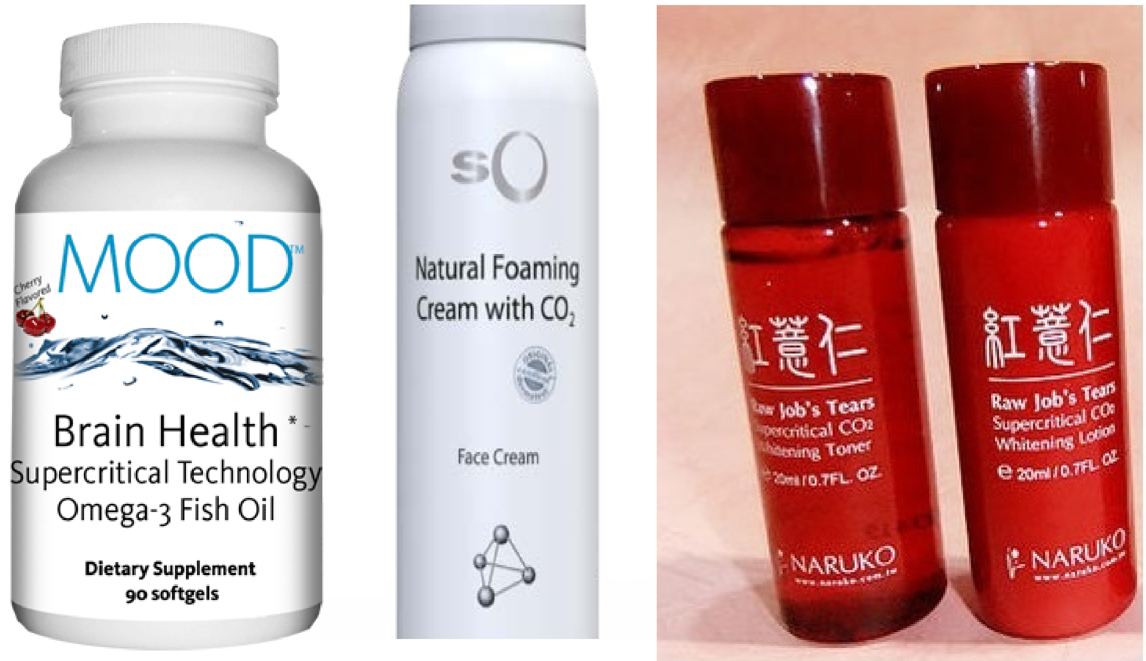
OVERCOMING THE "VALLEY OF DEATH"

One driver increasing the use of CFT is that it is the most acceptable and prevalent method to process certain materials. The most obvious successful example of this is the use of SC-CO_2 to obtain hops extract – which has become the worldwide standard for processing hops extract [3]. Other examples which could qualify include the extraction of astaxanthin from algae, processing of sawtooth palmetto berry extract, and possibly cannabis extraction. As pictured in Figure 1, low pressure carbon dioxide is becoming a prevalent method for cannabis extraction within the USA.

The development and availability of "portable" processing modules to demonstrate at a potential company's (customer's) site is another way of overcoming a barrier to consider CFT processing options. Callaghan Innovation in New Zealand [21] is using this approach to effectively integrate SFE and SFC in New Zealand; similar approaches have been used in Japan to demonstrate the effectiveness of subcritical water hydrolysis for waste conversions in several industries on-site at one ton/day capacities[27].

The development of national and international organizations intended to promote CFT can have a substantial impact - organizations such as Innovation Fluides Supercritiques (I.F.S.), FeyeCon, Flucomp, Taiwan Supercritical Fluid Association (TSCFA), Asian Society for Supercritical Fluids, ISASF, ISHA, Supercritical CO_2 Power Cycle (Power Cycle), Compressed Fluids Technologies, Critical Fluid Symposia (CFS) as well as various "green" chemistry organizations worldwide, such as the Green Chemistry Group which largely promotes supercritical fluid chromatography (SFC). The EMSF 2014 Bilateral technical and business meeting at EMSF 2014 is an excellent example of the promotion of the CFT platform.

Of additional importance is the identification on product labels that a supercritical fluid process has been used in producing the product. A number of examples of this will be made in the presentation particular in the area of nutraceuticals, cosmetics, and the food industry. Noted below in Figure 2 are several examples that "advertise" the use of CFT on products in the nutraceutical and cosmetic industry. It should be noted that there are examples of "false advertising" which occur under "supercritical" labelling and attacks on the CFT platform as being “unnatural” by the pressing and molecular distillation processors. Illustrations of this claim that “CO_2 is a chemical” and similar comments will be provided. For this reason, as noted below, certification that products have been produced using a genuine CFT process is important.



(a) (b) (c)

Figure 2: CFT products: (a) omega-3-fish oil concentrate, (b) face cream, (c) skin whitener

Perhaps more important is that some of these groups provide label certification that SC-CO_2, etc., on products produced using CFT. SAS Atelier Fluides Supercritiques in Nyons, France provides “certificat de conformite (ECOCERT)” to verify products produced by their processing schemes, similarly CO_2 – treated rice in both Taiwan and South Korea bear the SC-CO_2 processed label.

CONCLUSIONS

Additional promising CFT options continue to evolve even to a level of commercial acceptance. Among these are CFT dyeing of textiles, the promising area of bank note cleaning [28], and an array of hydrothermally-produced products for the catalyst, battery and solar cell component, biomedical applications such as sterilization, and the composites industries. To carry these promising applications into full commercial and sustainable development will require entrepreneurial scientists/engineers with training and an appreciation of the economic, industrial, and cultural factors throughout the world that impact on the success or failure of CFT. Excellent partnerships between government funded agencies and academic institutions have had significant impact in the nations of South Korea, Taiwan, and New Zealand. Perhaps one last comment would be in order regarding those anticipating commercializing CFT – it is absolutely imperative that one look at the “bigger picture”, which includes factors outside the technological platform such as the target industry, marketplace, and economics to assure success in the international application of CFT.

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