PGX Technology:
A Case of University – Industry Partnership for Innovation

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ABSTRACT

The PGX (Pressurized Gas-eXpanded liquid) Technology is a platform technology that is used to convert biopolymers into high-value materials overcoming the challenges associated with the drying of high molecular weight biopolymers using conventional technologies. Moderate PGX processing conditions, involving the use of CO_2+ethanol for water removal while precipitating the biopolymer, minimizes any potential degradation. Variation of the processing parameters results in dried biopolymers of very low bulk density in different forms (fine powders, microfibrils, fine or coarse granules etc.). Their high specific surface area allows them to be loaded with drugs or food-grade bioactives via adsorptive precipitation using supercritical CO_2 in a second step. Such delivery systems open up a wide range of possibilities for product applications, including functional foods, natural health products, cosmetics, personal care products, pharmaceuticals and others.

The PGX technology was developed at the University of Alberta and patented (U.S. Patent 9,249,266 (2016); Canadian Patent 2,794,960 (2016)) with the assistance of TEC Edmonton. It was then licensed to Ceapro Inc. for scale up and commercialization. The pathway from the lab scale at the University of Alberta to commercial scale at Ceapro required numerous contributions and was not straightforward. Nevertheless, the strength of the technology, which was based on solid science, and the identification of lucrative opportunities were crucial not only for the patenting process but also for raising the required capital to design, build and carry out scale-up trials. As a result of much work, Ceapro has built pilot scale and production scale units reaching commercial scale aqueous feed flow rates, thereby transforming laboratory findings into innovative products, which are the fruits of multidisciplinary collaborations and strong partnerships.

This partnership has led to ongoing research and development initiatives to expand the scope of this innovative technology. For example, PGX-dried oat β-glucan was loaded with CoQ10, a powerful antioxidant, which was used in the formulation of a functional beverage. The reduction in the crystallinity and particle size allowed uniform dispersion of CoQ10 in an aqueous medium, which otherwise is not possible.

A NOURISHING GROUND: UNIVERSITY OF ALBERTA

The supercritical fluid technology research program of F. Temelli at the University of Alberta focuses on the value-added processing of Canada's agricultural resources, specifically lipids and bioactive components with health benefits. Her program targets the use of supercritical carbon dioxide (SC-CO_2) technology, involving various unit operations, including extraction, fractionation, reactions, membrane separation and particle formation techniques with the goal of novel process development based on a solid understanding of fundamentals. The fundamental aspects deal with solubility behavior, and transport and physical properties under supercritical conditions. This involves the study of diffusivity, density, viscosity, melting point, interfacial tension and contact angle. Such properties are challenging to measure but essential for process and equipment design while enhancing our understanding of these systems. The core funding for this program is provided by the Natural Sciences and Engineering Research Council of Canada (NSERC), thanks to their Discovery Grants program, which is leveraged from other sources on specific applications. Having the flexibility of the Discovery Grant gives F. Temelli the opportunity to explore new ideas.

Another aspect of F. Temelli's research program focuses on grain fractionation with the goal of value-added processing of grains grown in Alberta. Fractionation of lipid, protein, starch and fiber components of cereals and pulses using dry and wet separation techniques, detailed characterization of the fractions obtained and developing product applications have been ongoing for more than two decades thanks to the funding support of provincial and producer organizations. A major focus of this program has been β-glucan isolated from oat and barley. β-Glucan is a soluble fibre component with health claims approved in many jurisdictions in the world indicating that it may reduce the risk of heart disease by lowering blood cholesterol.

B. Seifried completed his PhD program under the NSERC-Discovery Grant program of F. Temelli in 2010 [1] and was also funded by a scholarship provided by Alberta Ingenuity. Following his initial work on the determination of the physical properties of fish oil-saturated with CO_2, specifically density, viscosity and interfacial tension, the goal for the next step was encapsulation of fish oil using supercritical technology. Having purified fractions of β-glucan available in the lab from the grain fractionation project was beneficial to target it as a coating or carrier material. Initial attempts at different approaches to encapsulation were not successful but led the way to the modification of objectives. Having the broad multidisciplinary expertise and the flexibility in funding allowed us to focus on new opportunities. This led to the development of a two-step approach, where a biopolymer can be dried into nano-structured morphologies using the gas-expanded liquid mixture of water-ethanol-CO_2 in the first step, which can then be loaded with a bioactive in the second step. This new processing approach was successfully demonstrated for the case of β-glucan and gum arabic, and using fish oil and β-carotene as the bioactives.

Recognizing the potential of this new approach and to be able to move beyond a PhD thesis, it was necessary to ensure protection of intellectual property (IP) rights. Thus, a Report of Invention was filed with TEC Edmonton (www.tecedmonton.com), which is the commercialization arm of the University of Alberta. This was done just before B. Seifried's PhD thesis defense, which was attended by a Ceapro representative who immediately saw the potential of the technology and enticed B. Seifried to join Ceapro. A provisional patent application was filed on April 1, 2010, which was followed by a PCT application on April 1, 2011. From then on, additional work was conducted to gather the required funds to deal with the legal issues and to justify claims. All this work, along with support from Ceapro, led to the issuance of the Canadian [2] and USA [3] patents in 2016.

A SUPPORTIVE ENVIRONMENT: SCALE-UP AND DEVELOPMENT AT CEAPRO

In 2010, B. Seifried joined Ceapro Inc. (www.ceapro.com) in Edmonton with financial support for the first two years by an R&D Industry Associateship from Alberta Innovates Technology Futures (AITF). Ceapro is a biotechnology company focusing on the extraction of active compounds from natural sources and their utilization in innovative ingredients for the personal care and healthcare industries. One of the key bioactives driving Ceapro's business is β-glucan isolated from oats. The top management at Ceapro had very early on realized the great potential of this innovative technology, not only for their in-house bioactives but also for others. Therefore, in 2010, discussions were initiated between Ceapro and TEC Edmonton for the transfer of the biopolymer drying and impregnation technology to Ceapro. A licensing agreement was signed in May 2014, which was later amended in February 2015. This agreement gives Ceapro the exclusive rights for scale up and commercialization. The technology is now trademarked by Ceapro as the 'PGX Technology' identifying the use of 'Pressurized Gas eXpanded liquids' for drying of high molecular weight polymers.

As outlined below, numerous milestones and essential developments were achieved from 2010 to 2018. Indeed, during this time the PGX Technology was developed from lab-scale to pilot scale and production scale at Ceapro. Those steps included a wide range of activities such as designing and testing multiple nozzle prototypes and various other custom built components to scale-up the PGX equipment, reaching commercial scale aqueous feed flow rates, and at the same time preparation of numerous biopolymer samples, presentations at many conferences to network and look for potential partners in both academia and industry for application development, transforming laboratory findings into innovative commercial products.

When B. Seifried joined Ceapro in late 2010, Ceapro already had an R&D program and projects focusing on supercritical fluid extraction of bioactives, initiated by Paul Moquin, also a former PhD graduate of F. Temelli. The existing supercritical equipment available at Ceapro was modified and extended at that time by B. Seifried to further develop the PGX Technology at the lab scale. This system allowed B. Seifried to test many biopolymer samples. Further scale-up to pilot scale was partly funded by Canadian Agricultural Adaptation Program (CAAP), the Prairie Oat Growers Association (POGA) and the PEI Product Development Assistance. All this funding facilitated the research collaboration Ceapro established with the BioFoodTech Center in Prince Edward Island (PEI), where a larger scale pilot plant (2x12 L, Thar) for supercritical fluid extraction was accessible, allowing to scale-up and generate larger quantities of β-glucan samples for product development. In the years 2011 and 2012, with Ceapro's support, B. Seifried transformed the existing pilot scale extraction equipment at the BioFoodTech center in PEI into a larger PGX pilot system by the addition of pumps and auxiliary equipment to optimize various process conditions and test prototypes of custom designed nozzles and baskets. Furthermore, in 2012, the scale-up reached a level, which made possible the generation of several kilograms of PGX-processed β-glucan samples on that modified pilot skid in PEI. In 2012, with further scale-up in mind, Ceapro initiated a collaboration with CF Technologies Inc in Boston, MA, USA, a company specializing in development and manufacturing of custom-built supercritical fluid equipment. In collaboration with CF Technologies, further scale-up, focusing on equipment modifications and refined nozzle design was carried out on custom-built equipment in PEI and Boston with the aim to increase flow rates of the PGX process to commercial scale. Numerous prototypes and test trials were performed in the years 2012 to 2015 by fine-tuning processing conditions, nozzle and basket design.

In parallel to the equipment and process scale-up work, Ceapro tested PGX Technology on the lab scale on numerous well known biopolymers (starch, pectin, alginates, chitosan, nano-crystalline cellulose (CNC), etc.) and proprietary polymers from Canadian, international and multinational companies. Furthermore, in 2014, Ceapro financed and worked in collaboration with the Massachusetts Institute of Technology (MIT) and CF Technologies in Boston on an initial pilot study on the impregnation (adsorptive precipitation) of CoQ10 onto PGX-dried β-glucan. In 2014, funded by Alberta Innovates Bio Solutions (AI Bio) under the Food Innovation program, Ceapro initiated a collaborative research project with F. Temelli at the University of Alberta focusing on the development of a functional food ingredient, namely CoQ10 impregnated onto β-glucan, which resulted in the detailed characterization of the ingredient and formulation of a functional energy drink. Since the initial MIT study delivered promising results, it was therefore continued by a second study in 2015 at the MIT, where the scope was extended to impregnate CoQ10 onto PGX-dried β-glucan, starch, and pectin, as well as initial trials for impregnation of various APIs onto PGX generated biopolymer matrices in collaboration with CF Technologies in Boston. Furthermore in 2015, Ceapro purchased a used pilot plant for supercritical fluid extraction (UHDE, Germany), which has been modified and adapted to run further tests for scale-up and process optimization of the PGX Technology in Boston. As well, in 2015, Ceapro received a generous funding contribution of $800,000 from AI Bio towards the commercialization and scale-up of the PGX Technology, which aimed at building a demonstration plant at Ceapro Inc. capable of processing at commercial flow rates. Furthermore in 2015, Ceapro received financial support from the National Research Council (NRC) through its Industrial Research Assistance Program (IRAP) to support salaries of engineers and researchers that joined Ceapro in the years 2015 and 2016 for building a PGX team at Ceapro dedicated to the design and building of a PGX demo plant for processing a wide range of biopolymer feedstock.

A STRONG VARIETY: PGX TECHNOLOGY PLATFORM AND MULTIDISCIPLINARY COLLABORATIONS

The PGX Technology is a platform technology that can achieve different functions while converting common low-cost biopolymers into high-value materials. In particular, high molecular weight biopolymers dispersed in water, forming highly viscous solutions can be dried, which is challenging to do using conventional technologies. In this process, the aqueous biopolymer dispersion is pumped into a high pressure vessel through a co-axial nozzle together with CO_2+ethanol. The conditions are selected such that the mixing occurs in the single liquid phase region of the ternary phase diagram of the water-ethanol-CO_2 system. The use of CO_2+ethanol under moderate pressure and temperature conditions allows removal of water while acting as an anti-solvent to precipitate the biopolymer and avoiding any degradation. The process conditions allow water removal at single phase conditions, leading to vanishing interfacial tension, thereby, avoiding agglomeration due to capillary forces. The dried biopolymer is collected in the collection vessel after passing pure CO_2 to remove any residual ethanol. The particles have a very low bulk density and their nano-scale morphology ranges from fine powders, microfibrils, to fine or coarse granules and others, depending on the properties of the biopolymer and the processing parameters employed. For example, gum arabic formed spherical and amorphous particles while β-glucan resulted in fibrils and sheet-like structures [1]. The dried biopolymer particles have a high surface area, which allows them to be loaded with drugs or food-grade bioactives via adsorptive precipitation [4] using supercritical CO_2 in a second step.

Since 2010, Ceapro has been engaged in many research collaborations for developing the PGX Technology, starting with the scale-up at the BioFoodTech Center in PEI to transition from lab to pilot scale on a modified supercritical fluid extraction skid, followed by extensive scale-up and process optimization trials with an industrial partner (CF Technologies in Boston), along with collaborative research projects, involving academia such as MIT in Boston. As well, with Ceapro's support and additional research funding provided by the provincial and federal funding programs, it was possible to further scale-up and engage in many collaborations for applications development of the fine-structured biopolymer materials generated by the PGX Technology.

In that context, the first key research project initiated in 2014, based on the initial trials at the MIT, built on the existing partnership and close relationship between the University of Alberta and Ceapro and has triggered further research activities and projects at the University of Alberta, aiming to expand the scope of this innovative technology. For example, PGX-dried oat β-glucan was loaded with CoQ10, a powerful antioxidant, and a loading level as high as 18% (w/w) was achieved at 45 min recirculation time and a depressurization rate of 13 MPa/min [5]. Detailed characterization of the CoQ10-loaded β-glucan demonstrated the reduction in the crystallinity and particle size of CoQ10, which was uniformly distributed on the delicate fibrous structure of β-glucan [6]. This morphology allowed uniform dispersion of CoQ10 in an aqueous medium, which otherwise is not possible and led to the formulation of a functional beverage [7]. Continued research activity at the University of Alberta with funding from the Collaborative Research and Development Program of NSERC and Ceapro is focusing on various biopolymers and their loading with different bioactives for functional food ingredients, nutraceuticals and cosmeceuticals. The findings will contribute to our understanding of the behavior of different biopolymers under PGX conditions and their interactions with bioactives as well as the relationship between the processing parameters and the properties/functionality of the powders obtained.

Furthermore, since 2016 Ceapro has ongoing research collaboration with the Department of Chemical Engineering at McMaster University funded by an NSERC Strategic Grant, working closely with Professors Todd Hoare and David Latulippe on the development of highly tune-able porous biopolymer and smart polymer scaffolds, as well as drug delivery and purification applications. In 2016, Ceapro received NSERC Engage support for a project, focusing on the generation of cross-linked CNC aerogels utilizing PGX Technology for applications in bone-tissue scaffolding, working with Professor Emily Cranston at the Department of Materials Science and Engineering at McMaster University [8]. In addition to the application development of numerous PGX-processed polymers, Ceapro started a research project in 2016 funded by the German Canadian Center for Innovation and Research (GCCIR) in collaboration with two German Fraunhofer Institutes (IKTS and IAP) and one SME specializing in membrane processing equipment (A. Junghans, Frankenberg, Germany) with the aim to develop novel polymeric and inorganic membranes for the purification and dehydration of ethanol, which is utilized in the PGX process. Due to the existing expertise with polymeric membranes under supercritical fluid conditions, this membrane research project also involves F. Temelli and her group at the University of Alberta specifically for membrane testing and characterization. The development of novel membranes can lead to improvements of the PGX Technology at commercial scale as well as other new process developments and research projects.

The ongoing collaborations and research activities between Ceapro, various Universities, research institutes and industrial partners, connecting the expertise from multiple disciplines and even beyond national boundaries is key in advancing the process and application development for PGX Technology. Novel delivery systems for bioactives open up a wide range of possibilities for product applications, including functional foods, natural health products, cosmetics, personal care products, pharmaceuticals and others. Furthermore, the development of exfoliated nano-composites, cross-linked aerogels using multiple biopolymers and implementing other components can facilitate applications, ranging from wound-healing and bone tissue scaffolds, adsorption materials, 3D printing and supercapacitors, which could benefit from the plethora of unique nano-scale morphologies generated by PGX Technology. The numerous collaborations across multiple disciplines are key in cross-pollination of ideas driving innovation, which will lead to the development of novel ingredients, materials and processes for a wide variety of applications.

A FRUITFUL OUTLOOK

The key factors for success to transform a novel idea into a commercial success are comparable to those growing an apple tree from seed to harvest, which requires for seeding a great idea, a solid nourishing ground, a healthy supportive environment and a strong variety of collaborations that with the help of many skilled people along with patience and time will lead to a fruitful outlook. In the case of PGX Technology, we have been fortunate in all of the above key factors: A **nourishing ground**, in the form of the long-standing expertise at the University of Alberta on grain fractionation and supercritical fluid technologies. The supercritical technology program funding provides flexibility to explore new approaches. As well, the program leader allows new ideas to flourish. The above conditions were essential for the novel ideas to prosper and thrive in an academic environment leading to the development of the PGX Technology. For the transition from academia to industry, the support systems, such as TEC Edmonton must be in place to assist researchers in terms of intellectual property protection, legal agreements and technology transfer. Furthermore, a healthy **supporting environment** must be available in the form of a supportive industry partner such as Ceapro Inc. and all funding agencies, which are required to successfully transition a lab-scale technology or idea into a commercial scale opportunity. This transition also requires foresight and additional effort, endurance and courage by both the industrial partner and inventors. It takes entrepreneurial spirit, networking and presentation skills to find suitable industrial partners and collaborators along with the necessary financial support to de-risk the technology transfer, scale-up and commercialization. Financial support is needed at all stages of such technology development and transfer from academia to industry to enable continued research and development. The financial support is more accessible with “a **strong variety**” **of collaborations**, having strong partners and dealing with a versatile platform technology, such as the PGX Technology with its strong fundamentals that is likely to succeed and become applicable in a multitude of industries and applications. Finally, and most importantly, it is the “busy bees” or **many people involved** that turn ideas into action and make it all happen. Numerous collaborations across disciplines are best for cross-pollination of new ideas and driving innovation. In this case, success is possible thanks to the incredible teams of hard working individuals at Ceapro, University of Alberta, McMaster University, BioFoodTech, CF Technologies and within all the organizations who have chosen to invest into the advancement of this technology, covering all aspects from fundamental research to applied research in a multidisciplinary network.

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