Hanze
University of Applied Sciences
Groningen

Transition Bioeconomy

R.J.F. (Rob) van Haren

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Biorefinery of bioceuticals for new product development in the circular bioeconomy.

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Professor R.J.F. (Rob) van Haren (PhD)

Research Centre Biobased Economy

The research centre Biobased Economy of Hanze University of Applied Science in Groningen wants to contribute to a healthy and sustainable society. New and specific bio-based products, processes and activities are being developed in close collaboration with businesses, which therefore better fit the market demand.

This development takes place among others in the Zernike Advanced Processing (ZAP) facility. This is an innovative work-based learning environment where applied research and education is carried out in cooperation with industry, regional secondary vocational education centres (Noorderpoort and Alfa-college) and the University of Groningen.

The research centre Biobased Economy focusses on ingredients (like carbohydrates), new processes for green chemistry and green extraction of active plant ingredients. Applications are for pharmaceuticals, cosmetics and nutraceuticals(bioceuticals) and natural extracts for colors, flavors and fragrances.

Kenniscentrum Biobased Economy

Het kenniscentrum Biobased Economy van de Hanzehogeschool Groningen wil bijdragen aan een gezonde en duurzame samenleving. Door samen te werken met bedrijven worden concrete, nieuwe biobased producten, processen en bedrijvigheid ontwikkeld die beter aansluiten op de vraag van de markt.

Deze ontwikkeling vindt onder andere plaats in de Zernike Advanced Processing (ZAP) faciliteit. Dit is een innovatieve leer-werk omgeving waar toegepast onderzoek en onderwijs wordt uitgevoerd in samenwerking met het bedrijfsleven, regionale opleidingscentra (Noorderpoort en Alfa-college) en de Rijksuniversiteit Groningen.

De focus van het kenniscentrum Biobased Economy ligt op ingrediënten (b.v. koolhydraten), nieuwe processen voor groene chemie en groene extractie van actieve plantaardige inhoudstoffen. Toepassingen zijn voor farmacie, cosmetica en nutraceutica (bioceuticals) en natuurlijke extracten voor kleur, geur en smaakstoffen.

Forschungszentrum Biobased Economy

Das Forschungszentrum Biobased Economy der Fachhochschule Hanzehogeschool Groningen möchtet an einer gesunden und nachhaltigen Gesellschaft beitragen. Neue nachhaltigen biobased Produkte, Prozesse und Aktivitäten werden in enge Zusammenarbeit mit Unternehmen entwickelt, dabei sie besser an die Marktfrage anschließen.

Diese Entwicklung findet u.a. in der Zernike Advanced Processing Fazilität statt. Die Fazilität ist eine innovative arbeitsbedingter Lernumgebung wo angewandter Forschung und Ausbildung in Zusammenarbeit mit dem Betriebsleben, regionalen Bildungszentren (Noorderpoort und Alfa-college) und der Universität von Groningen ausgeführt wird.

Der Fokus des Forschungszentrums ist Zutaten (z.B. Kohlenhydrate), neue Prozesse für grüne Chemie und grüner Extraktion von aktiven pflanzlichen Inhaltsstoffen. Anwendungen sind für die Pharmazie, die Kosmetik und Nahrungsergänzung (nutraceuticals /bioceuticals) und natürliche Extrakte für Farbstoffe, Duftstoffe und Aromen.

Zernike Advanced Processing (ZAP) research facility for semi-industrial scale green processing technology and prototyping facilities for the circular Biobased Economy. ZAP is part of the Research Centre Biobased Economy.

Contents

1. Introduction

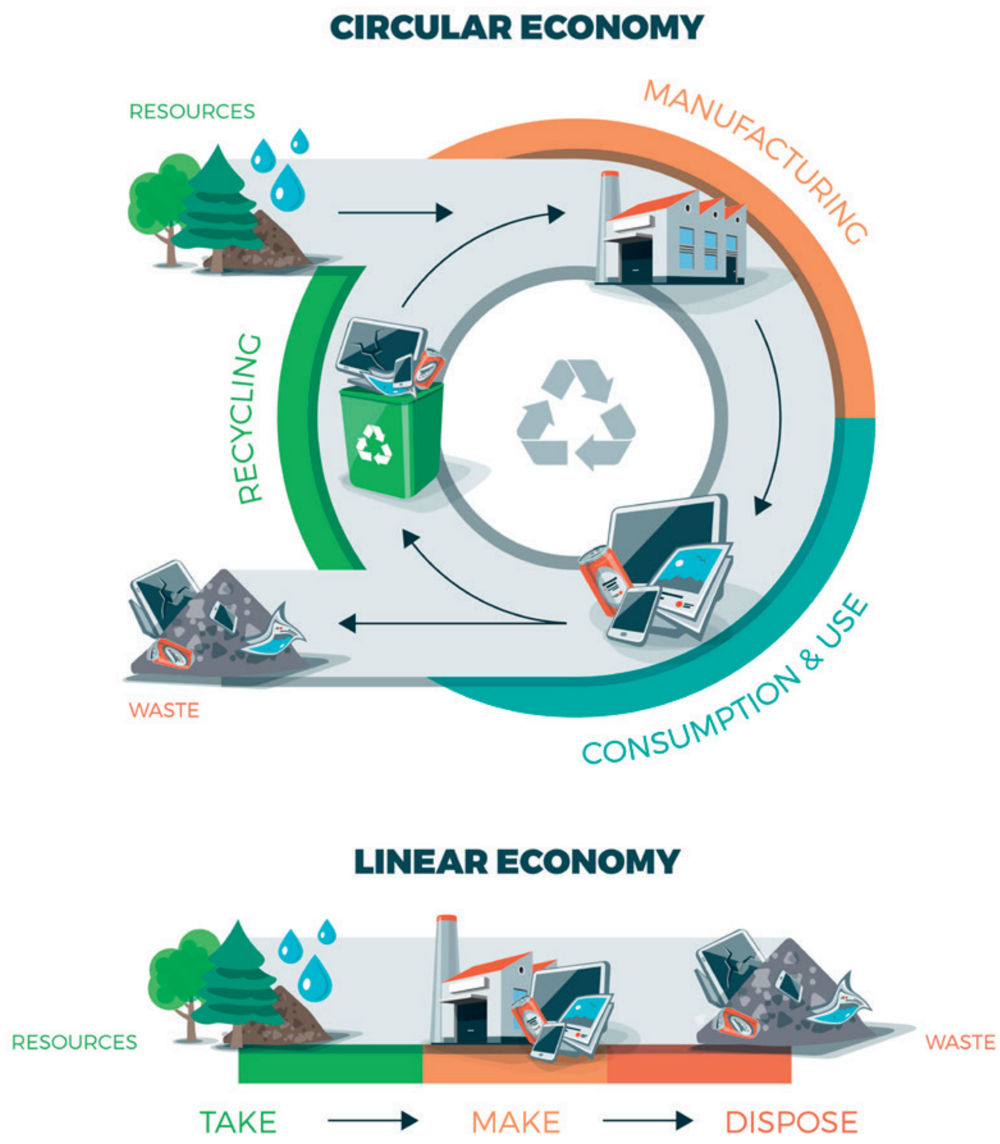
At the moment society is undergoing a desired transition into a sustainable, green bioeconomy. This transition is supported by citizens who wish to live in a sustainable society, by consumers who want to buy natural, healthy products and natural materials, by governments that support this transition with law, regulation and subsidies and by science and industry that apply biobased innovations in practice.

The bioeconomy is characterized by the use of renewable, natural resources for health, food, feed, biochemicals, materials and energy and by efforts to close material cycles by the recovery of non-renewable, raw materials, such as metals and minerals from renewable products. Bioeconomy and circular economy merge naturally together, creating opportunities for society, science and business. Bioeconomy is fuelled by the radiant power of the sun as the ultimate source of photosynthesis. Photosynthesis is the capacity of green plants to harvest and convert sunlight into proteins, sugars, lipids and secondary plant metabolites: the raw materials of the bioeconomy.

The biobased economy requires educated, well-trained people working for authorities, knowledge institutions, SME's and industries to contribute to this transition. The transition also requires new cooperation and business models, leading to co-creative innovations with added value for all these parties to apply in practice. Applied sciences bridge the gap between fundamental, curiosity-driven research by universities on the one hand and the needs of industries on the other hand, by means of interdisciplinary cooperation. This way fundamental knowledge can be applied to business needs and realised in practice for added value creation.

Hanze University of Applied Sciences (Hanze UAS) and the Institute for Life Science & Technology intend to facilitate this transition by initiating a new, interdisciplinary Research Centre Biobased Economy. Here, business, education and science meet in order to create sustainable biobased innovations. The Research Centre Biobased Economy facilitates semi-industrial, green processing technologies within the Zernike Advanced Processing facilities (ZAP) in Groningen, the Netherlands.

The circular bioeconomy is characterized by using renewable materials and by re-using non-renewable materials in contrast to linear economy where renewables and non-renewables are wasted.



2. Mission

The mission of the research group *Transition Bioeconomy* is to facilitate society and businesses in their transition to the bioeconomy, by merging business with applied research in life sciences and technology, with respect to biobased ingredients and green processing technologies. The emphasis is on new concept and product development with plant ingredients for pharmaceutics, cosmetics and nutraceutics (bioceuticals) as well as on green processing technologies, which are free from fossil-based solvents and use less energy, water and other resources. The research group aims to stimulate interdisciplinary collaboration, to encourage entrepreneurship and to distinguish itself in terms of unlocking natural ingredients and the development of applications. The emphasis is on new product and business development, based on plant ingredients, plant fibres, proteins and oils as well as on applications for pharmaceuticals, cosmetics, food, materials and energy. The research group supports the social transition to a bioeconomy and the positioning of Hanze UAS.

3. Circular Bioeconomy

The bioeconomy is based on green raw materials of plant and/or animal products. Unlocking plant components by biorefinery of biomass is an important step in the value chain. Mostly, these processes are based upon "fossil technology", using organic solvents from mineral oils with a simultaneous high energy consumption. The use of organic solvents has a negative impact on people and environment and contributes to climate change. New developments are focused on designing green biorefinery processes which do not harm people and environment and promote recycling biomass by-products (Raghavan et al, 2014; Pfaltzgraff & Clark, 2014). The development and scale-up of green extraction technology is now in the development phase of applied sciences. (Chemat, 2012). Industrial interest in green products and processes is presently increasing due to the growing customers' awareness and new guidelines from EU and USA (respectively REACH and GRAS), declaring green extracted products to be "natural ingredients" of pharmaceutical, cosmetic and nutraceutical products.

New extraction technologies create new extracted fractions that differ in functionality from traditionally extracted fractions. Pharmaceutical, cosmetic and food industries have great interest in new, "clean label" functional plant extracts. Developing functional bio-assays that allow rapid screening of fractionated plant substances is a requirement. Scientific research of the development of rapid screening assays is rapidly increasing, in particular the "bioassay guided fractionation" (Agarwal et al, 2014; Tan & Lim, 2015). Application of $scCO_2$ extraction and fractionation technology lead to new ingredients for pharmaceuticals, cosmetics and nutraceuticals. The effectiveness of these new extracts needs to be determined with respect to specific applications, such as prebiotics, oppression of inflammatory reactions, prevention of skin aging, prevention of connective tissue breakdown in joints and anticancer treatments (Sharma & Gupta, 2015).

Regarding functional fractionated botanical ingredients, New Product Development is the next step in the value chain. Recent research shows that formulation of cosmetic and nutraceutical products on the basis of active vegetable ingredients is a challenge and still in development (Gurib-Fakim, 2014).

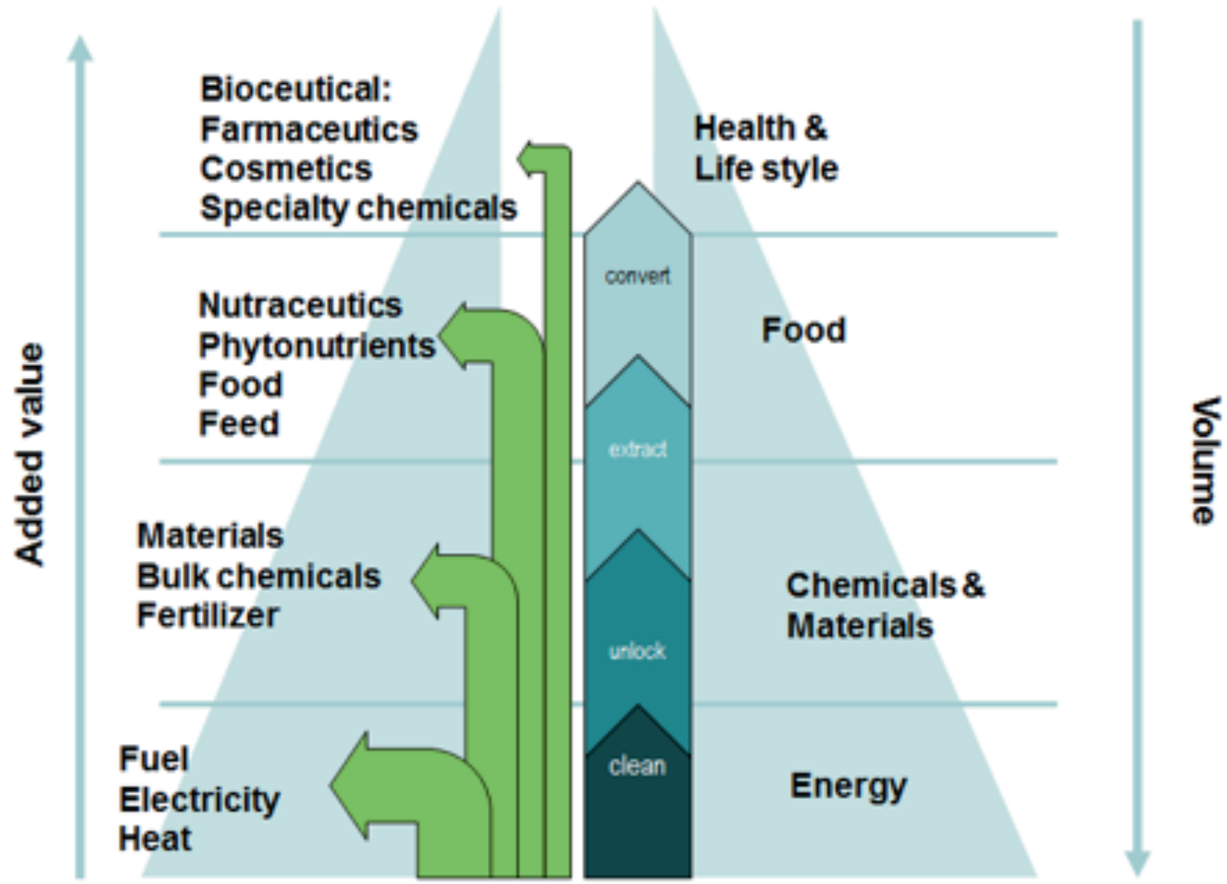
Biobased innovations and entrepreneurship form a research field that deserves attention, because of targeted growth strategies of the EU and national authorities. This field of research will be developed in the coming period and offers opportunities for extensive profiling. (Golembiewski et al, 2015; Schmid et al, 2012; Kirchner, 2012).

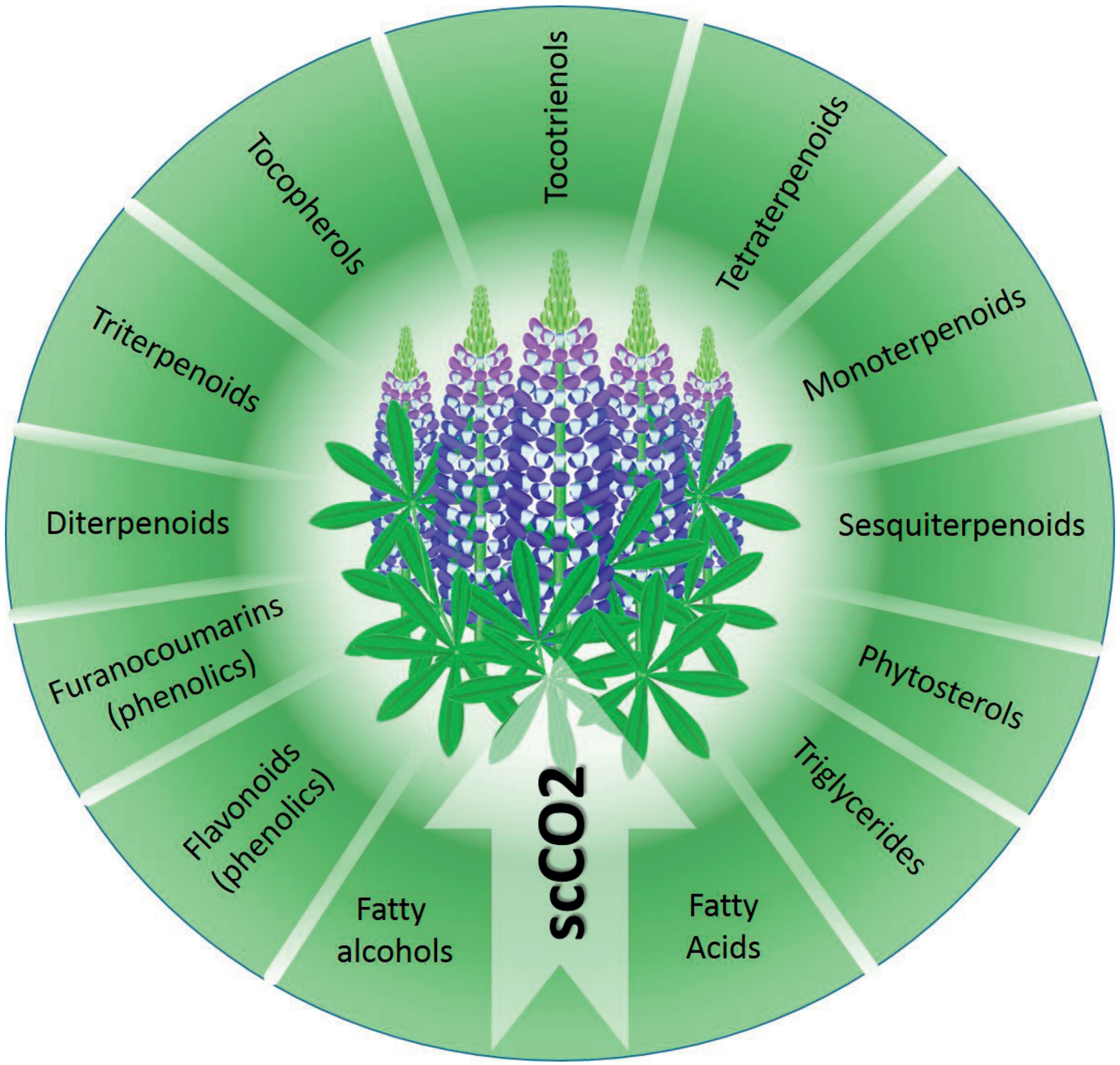
New business models are powered by the trend of downscaling and local production. Said new technologies enable the production on smaller local scale (possibly in rural areas, which increases the opportunities of new small business development and entrepreneurship. This trend matches the rapid growth of the chemical sector and the agricultural sector due to the increasing use of green raw materials in chemistry. The agricultural sector produces ten times as much rest materials as the chemical sector's global (future) need for biomaterials. The small scale also enables the transition from bulk to customization. The "old petrochemicals" are characterized by bulk and are cost-driven. The new economy of customization for the consumer's individual and personalized needs in the field of nutrition, health and lifestyle (personal health, personal nutrition and personal lifestyle) is characterized by specialty, added value and opportunities for entrepreneurship.

The value of biomass and green raw materials arises from the full exploitation of all components and ingredients, according to the so-called biocascading principle. The biocascading principle means using the most valuable materials and ingredients from biomass first, before finally converting the remainders into bio-energy. Biocascading means ordering biomaterials such as pharmaceuticals, cosmetics, fine chemicals, nanostructures, chemical building blocks and bioconstruction materials according to their added value levels in a range from medicine to nutrition to energy applications as green gas, biofuels for transport and last of all controlled burn capacity.

The agri-food, health and chemical sectors form important economic engines for the Netherlands. As a result of the presence of industries like Friesland Campina, Suikerunie, Cosun/Agrifirm, AVEBE and chemical industries such as DSM, BASF and Teijin in the area, the Northern Netherlands plays an important role. In addition, many SME companies and strong SME clusters in Germany and the Northern Netherlands are active in the domains of pharmaceutics, biomaterials, (red and white) biotechnology and agri-food.

Biocascading pyramid for added value of biomass versus volume of biomass





Supercritical CO2 extraction of secondary plant metabolites (after Melo et al 2014)

4. Vision and goals of the research group

The research group *Transition Bioeconomy* encourages entrepreneurship and innovations in the bioeconomy. The research group achieves these goals by teaching and carrying out interdisciplinary applied research regarding entrepreneurship and exploitation of biological raw materials, using green technology and the development of new products, applications and enterprises. Emphasis is on applications for pharmaceuticals, cosmetics and nutraceuticals, extracted with green technology from various biomass sources.

The research group will focus on the concept of "New Product Development by biorefining bioceuticals from biomass resources". This concept leads to three research lines. The first research line focusses on biorefinery of bioceuticals by means of green extraction technologies from biobased materials. The second research line is to determine the functionality of bioceuticals and the development of related products. The third research line aims at "New Product Development" in the bioeconomy:

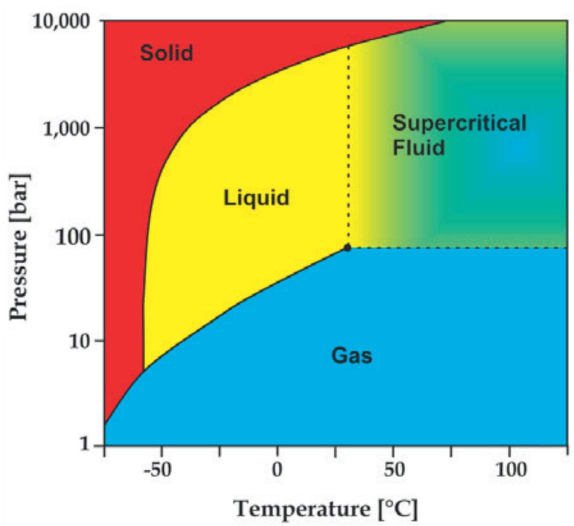
1) Transition Green processing technologies: this line focusses on the development of new biorefining processes for biomass and botanical ingredients by means of green extraction.
2) Transition Green ingredients and products: this line focusses on the development and evaluation of new products and services based upon ingredients (bioceuticals) from biorefining processes.
3) Transition Green entrepreneurship: this line supports starting and current entrepreneurs in their transition to green business by "conceptuation" which strengthens "New Product/Service Development" by design thinking.

4.1 Green extraction unlocking plant potential for the biobased economy

The first line of research is focused on biorefining vegetable ingredients, using green extraction technology. "*Green extraction is based on the discovery and design of extraction processes which will reduce energy consumption, allows use of alternative solvents, and ensure a safe and high quality extract/product*" (from Chemat et al, 2015). Supercritical fluid extraction (SFE) and supercritical fluid fractionation have recently attracted new attention, because SFE and SFF are on the verge of becoming commercial applications, partly as result of their potential as green extraction technologies (King 2014 and Melo et al, 2014). Extracts of plant species have been studied using supercritical fluid extraction(SFE) technology. Many extracts and pure components of these species are already in use for human nutrition and health purposes. New applications involve plants, of which the knowledge has not yet been fully exploited, but which already offer promising new opportunities for science and business. The interest of science and business in this SFE and SFF technology is driven by the great versatility of carbon dioxide as a green solvent. Its properties can be tuned by pressure, temperature and flow rate, in order to provide extracts with desirable compositions (selectivity enhancements). Other solvents (e.g. hexane, ethane, propane) have also been object of research but because of their use GRAS or REACH regulations do not permit them to be declared as natural materials (adapted from Melo et al, 2014,).

Natural plant compounds can be extracted by SFE and purified by SFF depending on the molecular properties of the target molecules. Extraction efficiency of supercritical CO2 extraction and fractionation processes depends on the molecular properties of the compounds, which affect solubility. Solubility of molecules in supercritical CO2 depends on pressure and temperature of the solvent, see phase diagram of CO2 below. (Perrotin, 2011).

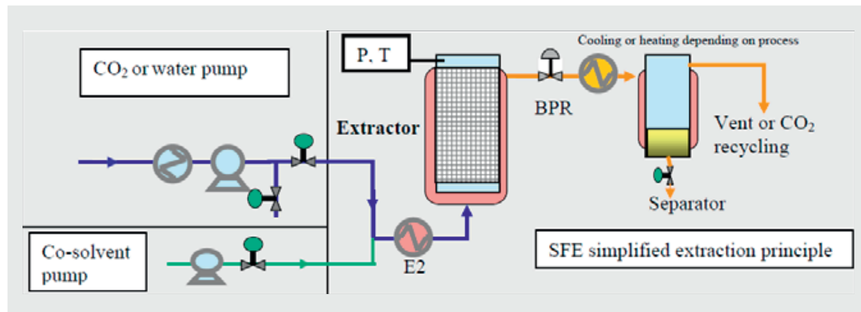
Phase diagram CO2



The research on the development of scCO2 extraction is focused on the dynamic interaction between biomass matrix and the behaviour of fluids under high pressure and temperatures. This research will provide knowledge for the techno-economical evaluation of green extraction by SFE and SFF, which is relevant for businesses that intend to undergo their transition to green technologies. An important problem in the industrial application of the green extraction technology is scaling up these technologies into feasible opportunities for industries. Scaling-up processes from laboratory to industry requires a combined approach of practical tests on semi-industrial scale, combined with in-silico simulations of industrial scale processes. Techno-economical evaluations of new business opportunities are hence supported by practical experiments and simulations with decision support systems. Several predictive models for SFE extraction have already been developed, using molecular characteristics of molecules and multiple authors have contributed to the properties of the plant matrix. (e.g. Zhen et al, 2012; Sovová, 2012b).

Research into processing technology and business management is prerequisite for a proper techno-economical evaluation of the technologies. Valle (Valle et al, 2014, Núñez and Valle, 2014) and Rosa and Meireles (2005) proposes a rapid evaluation scheme based upon extraction time, extraction efficiency, investment, energy and other costs. This rapid evaluation scheme proved to be successful. Valle (2014) proposes to refine the evaluation procedure by introducing mathematical simulation of the processes for studying technological constraints "in silico" for evaluation of scaling-up processes. Technical constraints regarding particle size, increase in scCO2 velocity and decrease in extraction time affect permeability of the substrate and thermal effects during reconditioning of extraction vessels. These effects limit the extraction rate and hence the economic viability of SFE. Valle (2014) advises close collaboration with industries in order to tackle scaling-up problems and refining estimates of plant costs as function of their size and configuration. The suggested models, in combination with empirical data gathered in experimental settings on laboratory and semi-industrial scale SFE units, will serve as the core of the new decision support systems. These systems will be developed further within the research group *Transition Bioeconomy*.

Graphical representation of laboratory and semi-pilot scale supercritical fluid extraction (SFE) facilities within Zernike Advanced Processing (ZAP) facility at Hanze UAS



4.1.1 Deoxypodophyllotoxin from wild chervil

Podophyllotoxin is the precursor of many pharmaceutical relevant products, such as etoposide and teniposide. Etoposide and teniposide are anticancer chemotherapy drugs. Etoposide is used in the treatment of testicular, bladder, prostate, lung, stomach and uterine cancers. Teniposide is used to treat acute lymphocytic leukaemia. Podophylltoxin is isolated from the Himalayan Mayapple *Podophyllum hexandrum*, which grows in the Himalayan mountains. *Podophyllum hexandrum* has become an endangered plant species, due to intensive wild gathering and harvesting of the plant. Cultivation of this plant is not yet possible, hence alternative sources for the production of podophyllotoxin have to be found. Podophyllotoxin content of collected rhizomes of *P. hexandrum* in the Himalaya ranged from 0.012% to 5.480% (Pandey et al, 2015).

Deoxypodophyllotoxin (DOP) is a compound very similar to podophyllotoxin. DOP can be extracted from the plant *Anthriscus sylvestris* (wild chervil, *fluitenkruid* in Dutch, *wiesenkerbel* in German) where it is found in concentrations up to 0.78% in mountainous areas or up to 0.15% in Dutch field conditions (Hendrawathi et al, 2011). Other studies showed concentrations of 2-3% of root dry weight (Koulman et al, 2001). Chemical and bioconversion routes for DOP to podophyllotoxin exist (see e.g Seegers et al), so wild chervil can be used as precursor for the anticancer drugs etoposide, teniposide and etophophos. Hanze UAS students have demonstrated the feasibility of SFE extraction of DOP from dried wild chervil roots. They achieved extraction efficiencies up to 90-95% of DOP from roots. A preliminary techno-economical evaluation of the DOP production business case in the Northern Netherlands showed promising results. The research was part of the INTERREG-EDR funded project Phytosana in cooperation with University Groningen and Syncom B.V.

Anthriscus sylvestris cow parsley, wild chervil, fluitenkruid, wiesenkerbel as source of deoxypodophyllotoxin

PhytoSana
INTERREG - Grenzregionen gestalten Europa
Europäischer Fonds für Regionale Entwicklung der Europäischen Union
INTERREG - Grensregio's bouwen aan Europa
Europees Fonds voor Regionale Ontwikkeling van de Europese Unie
EDR
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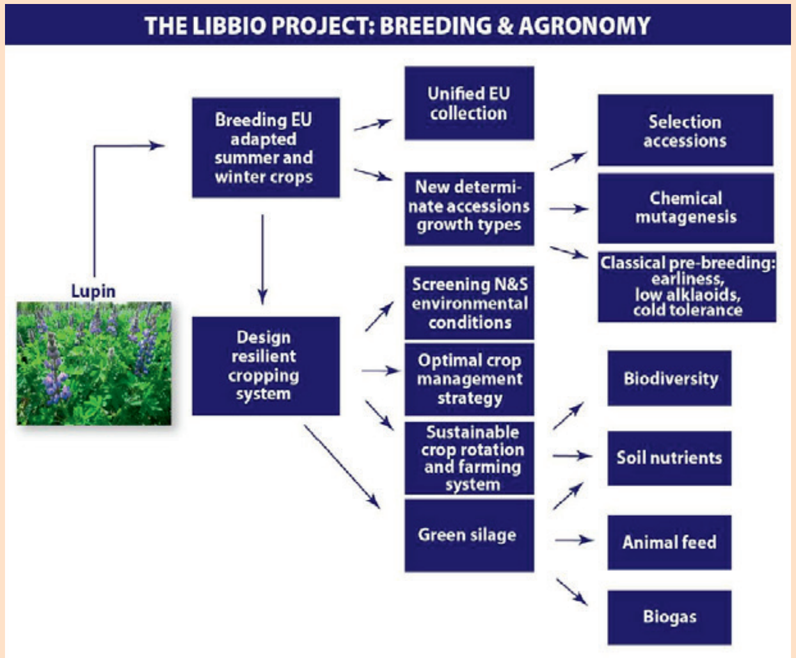
4.1.2 LIBBIO: Lupinus mutabilis for increased biomass from marginal lands and value for biorefineries

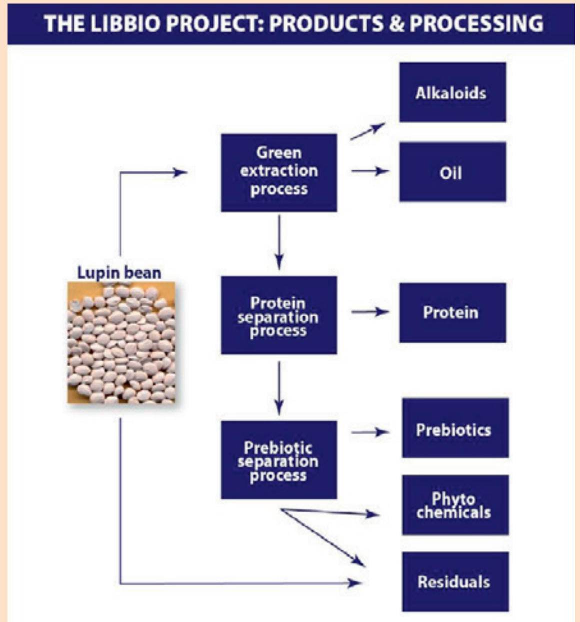
The LIBBIO project is about researching the potential of Andes Lupin for breeding cropping and biorefinery. 14 partners from 8 different EU countries cooperate together within the Horizon 2020 financed Research and Development program from the European Union for the Biobased Industries (BBI). Hanze University of Applied Sciences is technical-scientific coordinator of this 5 mio project. The project is from 2016 to 2020.

The Andes Lupin (Lupinus mutabilis, tarwi) grows excellently in marginal lands due to its excellent foraging characteristics having the ability to fix nitrogen, mobilise soil phosphate and have low nutritional requirements for cultivation. For the increased biomass needed in Europe in coming years and decades we cannot rely on the most fertile lands, which is currently allocated to food production, we need to increase the yield from marginal lands. There the lupin varieties are preponderant, the one providing highest yield is Lupinus mutabilis. Varieties can be chosen for giving this high yield of green silage or high yield of seeds contain more than 20% oil, more than 40% protein and the remainder carbohydrates are mainly oligosaccharides characterized as “prebiotics”. Andes lupin can be grown as a summer crop in Ncentral Europe conditions and as winter crop in Mediterranean conditions. Breeding and cropping research is performed in the LIBBIO project



for maximizing the yield and value of lupin agriculture in different European marginal lands conditions, with respect to both the farmers and biorefineries. Pre-industrial processing is developed and optimized for the lupin, properties of the different fractions analysed, their advantage for different industrial use evaluated, and a few products developed as an example. With respect to environmental impact the lupin is expected to be superior. It does not need much fertilizer, it enriches the soil with nitrogen and phosphate and is therefore expected to be excellent for crop rotation and soil regeneration. These properties will be evaluated further in the project along with techno-economic and agricultural viability and effect on farm and biorefinery income.

Hanze UAS will develop within this project an integrated biorefinery with supercritical CO_2 technologies. An integrated process will be developed for oil, protein and phytochemical extraction and fractionation. The techno-economical evaluation by Hanze UAS will be the base for future business development for Andes lupin processing.



European Commission
HORIZON 2020
The EU Framework Programme for Research and Innovation

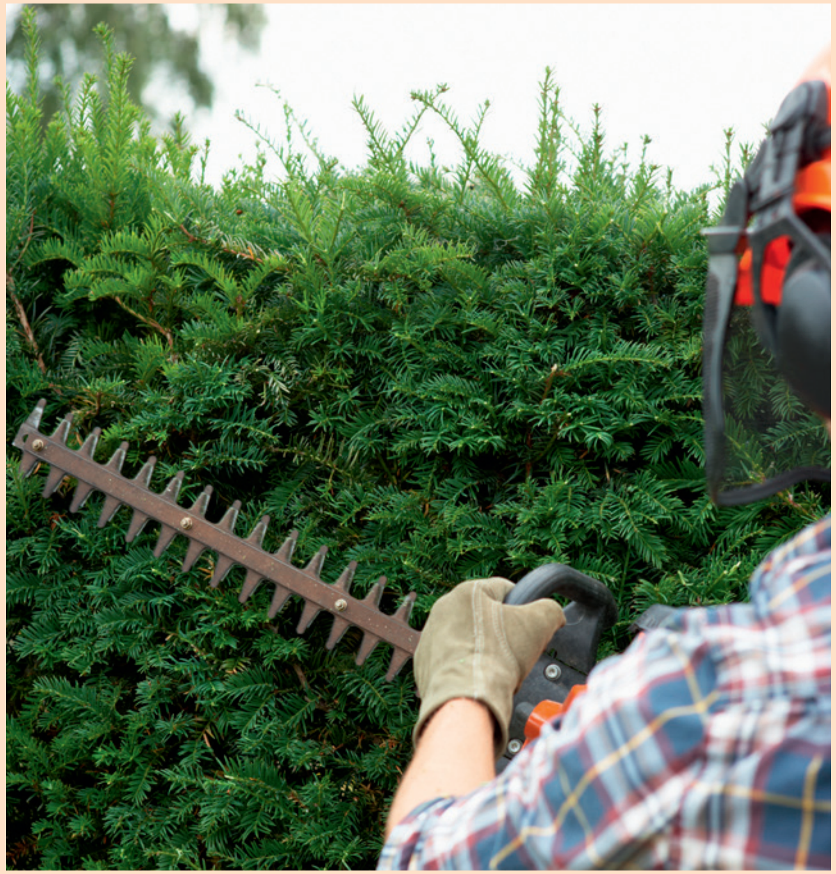
4.1.3 Lutein from lupin or marigold

Food enriched with nutraceutical ingredients may contribute to the prevention or postponement of (age) related diseases. Such a disease is age-related Macula Degeneration (AMD), an eye disorder resulting in distorted and blurred vision. Possibly, the effects of nutrition can contribute to the prevention of this particular disease. Scientific research suggests that a daily uptake of lutein and/or zeaxanthin may prevent or postpone the AMD disease incidence. The recent AREDS2 study showed positive effects of lutein, delaying the progress into late stage AMD (https://nei.nih.gov/areds2/PatientFAQ). Lutein is found in lupin seeds, fresh vegetables, potatoes and marigold (Tagetes spp). Potato fruit juices, the by-product of potato starch processing, is rich in glycoalkaloids, flavonoids and flavonoid lutein. Marigold flowers are also a source of lutein. Hanze UAS students have researched various extraction methods and found that supercritical co-solvent extraction (scCO2 with vegetable oil as co-solvent) can extract lutein from different botanical sources.

Lutein from Marigold for Age Related Macula Degeneration AMD prevention

4.1.4 Paclitaxel from European Yew

Paclitaxel (Taxol) is an important anticancer drug, which was first isolated from the bark of the Pacific yew. (*Taxus brevifolia*) (Wani, et al, 1971). Paclitaxel is one of the most powerful anticancer medicines of botanical origin. Yew trees grow extremely slowly, so alternative sources for paclitaxel or its precursors have to be found. European yew needles (*Taxus baccata*) are an important source of paclitaxel and other taxoid-related compounds. In turn these can be a source for semi-synthetic paclitaxel production. A new supply chain is developed in cooperation with SME companies and local authorities. Companies like Donkergroen B.V. and Syncom B.V. are working together with the research group *Transition Bioeconomy* on SFE extraction and SFF purification of taxoid compounds from European yew trimmings. Subsequently, Syncom B.V. will use these trimmings as raw materials for new semi-synthetic production of paclitaxel and paclitaxel derivatives.

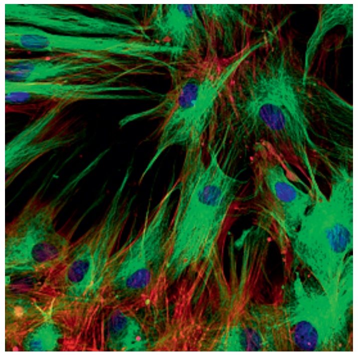


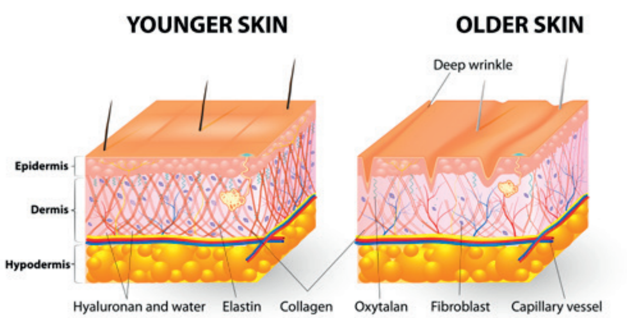
Taxus baccata trimmings for paclitaxel extraction

4.2 Green ingredients: new biobased ingredients and products

The second research line is to develop effective pharmaceutical, nutraceutical, cosmeceutical and cosmetic products based upon biobased bioceutical ingredients. This research line consists of two routes. The first is to establish the efficacy of extracted botanical ingredients (fractions) with bio-assays. The second research route focusses on the formulation of these extracts in enhanced extract/drug delivery systems and consumer products. The functionality of SFE extracted components and fractions needs to be underpinned by demonstrating their activities in dedicated bio-assays: bioassay-guided-fractionation. Purification of the active compound is realised by repeating SFE and SFF processes on the fraction that was tested positive (Han et al, 2015). Hanze UAS is developing a toolbox for bio-assay guided fractionation. Bio-assays can be used for cell-apoptosis (anticancer), collagen growth promotion and collagen breakdown inhibition with human skin fibroblast cell cultures (anti-aging skin care) and longevity tests with the nematode *Caenorhabditis elegans* for nutraceuticals.

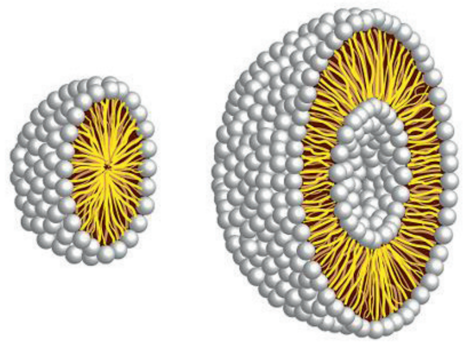
Human skin fibroblast bio-assay with immunofluorescence techniques to determine collagen synthesis and prevention collagen breakdown by inhibiting Matrix Metalloproteinase formation

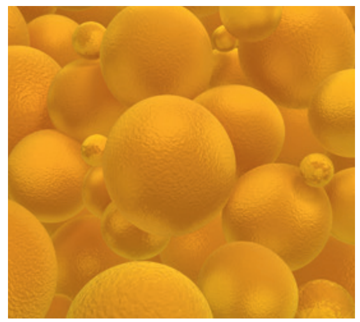




Lipid-rich (side) streams from vegetable processing contain a valuable group of components which attract both water and lipids:lecithins. Lecithin is a naturally occurring mixture of diglycerides of stearic, palmitic, and oleic acids, linked to the choline ester of phosphoric acid, and is found in living plants and animals (Wenninger et al 2000). Lecithins are applied as emulsifiers in food, pharma and cosmetics. Lecithins can be used in innovative applications as stabilizers for liposomes or, more recently, for nanostructured lipid carriers (NLC). NLC's are colloidal drug carrier systems that can be used for controlled drug delivery via various administration routes, such as oral or topical (skin) administration. Nano-encapsulation allows protection of sensitive bioactive ingredients and improves its bioavailability. The research group *Transition Bioeconomy* intends to develop nanostructured lipid carriers with lecithins, extracted from different botanical sources. Formulation of NLC is achieved with supercritical and subcritical particle formation processes, high pressure homogenization or micro-emulsion extrusion technology.

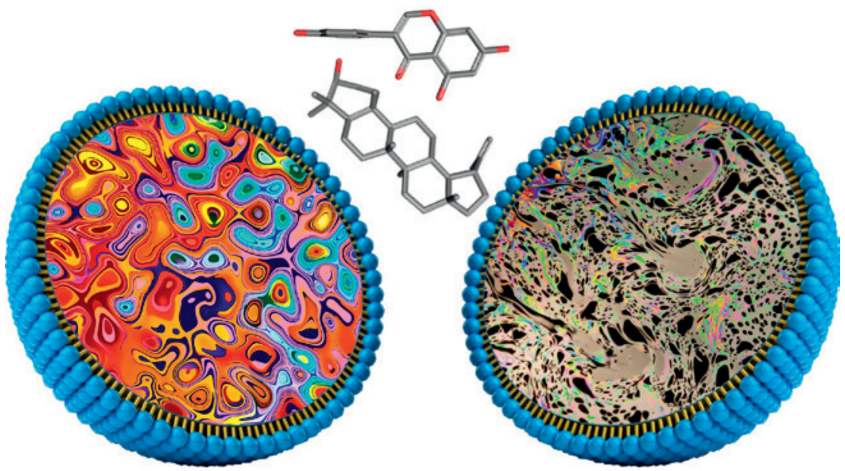
Solid Lipid Nanoparticle (SLN) or Nanostructured Lipid Carrier (NLC) (left) and liposome (right) as vehicles for safe controlled delivery of contained active components at the target site





New product development using botanical ingredients occurs in the field of cosmetic skin care formulations. Formulation technologies are developed which incorporate traditional methods based upon the HLB system (Hydrophile-Lipophile Balance), incorporating innovative nanostructured lipid carriers. The HLB system facilitates selection of proper emulsifiers in relation to selected (vegetable) oils in order to develop stable oil in water (o/w) or water in oil (w/o) emulsion systems. NLC's will formulate in the oil phase of the emulsions and will enhance controlled delivery of active botanicals into the skin. Efficacy of botanical actives and nanostructured delivery systems will be assessed with non-invasive in vitro skin measuring technologies such as skin elasticity, skin hydration, trans-epidermal water loss and skin surface topography (skin micro-relief). These techniques are non-invasive and can be employed by students. Thus the complete value chain for cosmetic product development can be evaluated: green extraction of active botanicals → purification of active botanicals → in vitro evaluation of active botanicals → protection and enhanced delivery of active botanicals by nanostructured lipid carriers → formulation in consumer skin care products → in vivo evaluation of efficacy of active botanicals.

Artist impression of nano-structured lipid carriers (NLC) with different semi-crystalline cores enriched with genistein and lupeol for improving respectively collagen synthesis and prevention collagen breakdown



4.2.1 Lupin seed extracts for anti-aging cosmetics

Lupin seeds are a rich source of proteins, peptides and secondary plant metabolites. Lupin attracts more and more interest, because of its high quality profile of proteins and oligosaccharides for human consumption. Lupin seed extracts contain significant amounts of bioactives such as polyphenols (isofavlones), carotenoids, phytosterols, tocopherols, alkaloids and peptides, which contain anti-oxidant, anti-carcinogenic, anti-microbial and anti-inflammatory activities (Kahn et al, 2015). Especially the triterpene lupeol and the isoflavone genestein have important skin caring properties by collagen protective and collagen stimulating activities respectively. As part of the Phytosana project, Hanze UAS has studied the collagen stimulating and protecting activities of lupin seed extracts with the skin fibroblast bio-assay. Lupin seed extracts and lupin peptides were kindly provided by ZoiY herbal cosmetic. The ZoiY lupin seed extracts and peptides showed a dose-response dependent activity of collagen stimulation and protection respectively. The research was part of the INTERREG-EDR funded project Phytosana.

ZoiY herbal cosmetic with lupin seed extracts, www.zoiy.eu

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4.3 Green entrepreneurship: new concept development by conceptuation

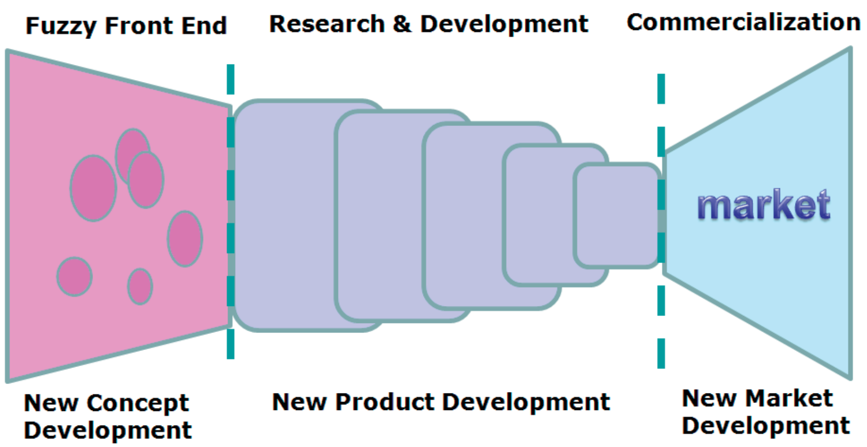
The third line of research concerns entrepreneurship and innovation. The research line focused in particular on new product and new business development, by structuring the early phase of innovation, the so-called fuzzy front end. In the early phase of innovation ideas are born and converted into specific prototypes, business or project plans. Usually processes in this phase of innovation are chaotic by nature and decisions are made on an ad hoc basis.

Innovation is something new with added value put into practice. The innovation funnel is a frequently used metaphor to describe the innovation process. Ideas are collected in a funnel, selected and subsequently developed into new products and services to be introduced on the market. The innovation funnel has three characteristic phases: concept development, product development and market development. The early phase of innovation or the fuzzy front end determines for almost 80% the success of the results, while only 20% of the resources are allocated to this phase. Most public and commercial organizations pay relatively little attention to this early phase of innovation, because of its unstructured and often chaotic process. Market success can be increased and costs and resources can be reduced by paying more attention to the fuzzy front end of innovation. The conceptuation method structures the chaotic fuzzy front end of innovation and hence reduces the time it takes to introduce a new product or service on the market.

The conceptuation method combines methods of design thinking, developed by Koen et al (2002) with the effectuation theory developed by Sarasvathy (2001). The conceptuation method attempts to structure the fuzzy front end of innovation and to accelerate innovation processes. The method accelerates the innovation process of new business and service development by sensing, idea creation and concept development. It structures, accelerates and increases the effectiveness of processes in the early phase of innovation, in order to achieve successful innovations in the market. The method was developed and applied previously in several domains, such as robotics, food product development, energy production, rural tourism and new services for adult learning and education. The conceptuation method was developed in close cooperation with Irmgard Starmann from Color&Brain B.V. and was applied as innovation method within the INTERREG project DANTE (http://danteproject.eu/). The method was selected as an example of a good practice within INTERREG EUROPE (IVc).

Koen et al (2002) combined a number of techniques in a coherent toolbox in order to structure the fuzzy front end. The conceptuation toolbox was enhanced with TRIZ methodology for solving "wicked" problems" (see BOX). Decision rules are based on effectuation principles. Actually, they represent how entrepreneurs will act when the future is unknown and the situation uncertain. The main principles are based on affordable risk and the mutual trust of actors, who act on the basis of what is available and see opportunities in unexpected events. Sarasvathy combines

Innovation funnel with three innovation phases



entrepreneurship and design thinking to create new ideas, opportunities and concepts. Design thinking is defined here as a mental process and as activities focussed on the development of new ideas, products and services. These principles are leading in the development of new tools for the fuzzy front end. Specifically, this concerns researching, developing and validating the toolbox by Koen et al and applying it to start-up and current entrepreneurs, with the objective to speed up innovation in these companies and structures.

The conceptuation method was developed based upon the theories, research and approaches mentioned above and prototyped in practice in collaboration with several companies, regional and national authorities and knowledge institutes. This resulted in a robust operational approach, leading to the creation of new concepts in an entrepreneurial setting. The conceptuation method consists of three major steps: opportunity, idea and concept. Within these steps we apply divergent and convergent thinking patterns as in the creative problem solving method developed by Osborn and Parnes.

The conceptuation method is a multi-disciplinary approach, enabling several disciplines and different stakeholders to work together, creating new ideas. Conceptuation workshops are facilitated by a creative facilitator and a creative challenger.

The conceptuation method leads to the following activities:
1) Opportunity identification and analysis
2) Idea creation and selection
3) Concept creation and description (scoping)

Each activity has its own specific tools. The tools of opportunity identification are based upon systematic analysis and sensing. Creative techniques form the tools of idea creation and selection. Finally, the tools of concept creation and selection are the standard financial and marketing techniques, combined with quick scans. Concept selection tools are derived from portfolio management.

Conceptuation starts with a lead or a question (from the market) and ends with a portfolio of different detailed concepts for further business development or new product development by entrepreneurs.

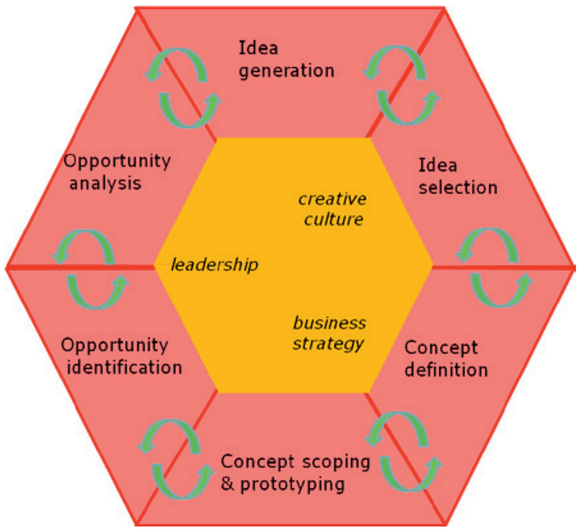
The analysis phase consists of identifying and analysing possible opportunities by analysing current products (voice of product), current customers (voice of customer), emerging technologies (voice of technology) or possible future developments (voice of future). The results of the analysis phase form the inspiration and starting points for the idea phase.

The idea phase consists of generating and selecting promising new ideas for business and product development. The idea phase consists of a diverging phase, when as many ideas as possible are created and a converging phase, when ideas are selected, combined and enriched. The selection process takes place against the background of the vision and strategy of the organization.

The selected ideas form the raw materials for the concept phase. During the concept phase ideas are transformed into pre-concepts and specific plans for new business and products. Techniques of enrichment and association are used to combine the results of the analysis phase with the selected ideas into fertile pre-concepts. Pre-concepts are developed during the concept phase into actual project plans and/or business cases and combined in a portfolio of promising new products or services.

The final results of the conceptuation method are identified and quantified business or product concepts upon which it is possible to justify strategic business or project decisions or develop policies.

Phases of conceptuation method for the Fuzzy Front End (after Koen, 2002)



4.3.1 Conceptuation workshop with INTERREG DANTE project

The INTERREG IVc project Dante (Digital Agenda of New Tourism approaches in rural and mountain areas) used the conceptuation method successfully. The method was introduced in transnational workshops with representatives of regional authorities, knowledge institutes and SME's in a triple helix setting. The objective was to develop new ICT concepts for the incorporation of context and location-sensitive social media tools into touristic service ICT portals for the end user and for touristic service providers. The results were used for the development of an open source toolbox for touristic service portal development.

The conceptuation method was selected by the INTERREG Europe secretariat and presented by Irmgard Starmann at the capitalisation workshop of selected good practices in Brussel in May 2014, marking the end of the INTERREG IVc programme (http://www.interreg4c.eu/policy-sharing-policy-learning/speakers/).

Transnational Dante project triple helix conceptuation workshop for developing new touristic service products (Bremen-Verden Germany, July 2012)

4.3.2 TRIZ problem solving toolbox

TRIZ is a problem solving toolbox developed by the Russian inventor and science fiction writer Genrich Altshuller (1926-1998). TRIZ (/ˈtriːz/; Russian: теория решения изобретательских задач, teoriya resheniya izobretatelskikh zadach) stands for "the theory of inventive problem solving". The basic principle of TRIZ is the discovery of "standard problems" and "standard problem solving solutions". This discovery was based upon the painstaking analysis by Altshuller and his co-workers of patent literature about recurring patterns. Altshuller started with analysis of many occurring problems in patent literature where he made the following observations

- problems and solutions are repeated across industries and sciences
- patterns of technical evolution are also repeated across industries and sciences
- the innovations use scientific effects outside the field in which they were developed

These observations were by Altshuller transferred into the fundamental TRIZ principles:

1) many problems are based upon a few solving principles
2) solving the intrinsic contradiction of the specific makes innovative solutions possible
3) (technological) systems evolve according predefined patterns intrinsic in the technology itself

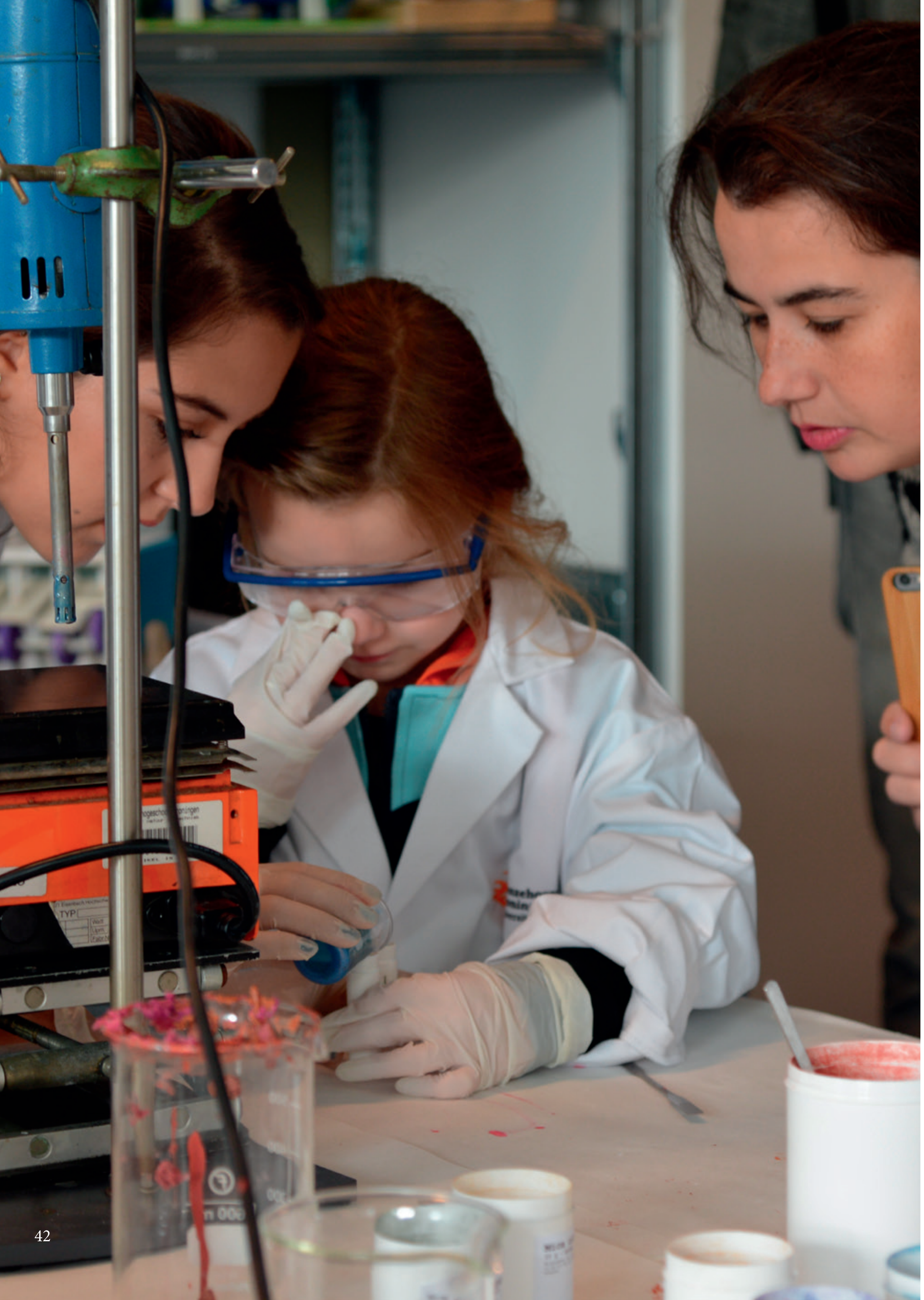
Based upon this analysis he deduced standard solution patterns based upon solving contradictions. These contradictions are the abstracted standard problems from the specific problem in case. His research resulted in a system of different problem solving tools. The art, creativity and science of TRIZ is based upon defining the ideal situation, in depth analysis of the problem, finding the contradiction in this problem, abstraction of the specific problem into one of the standard contradictions (problems) and finding the matching standard solution(s). Next step is to analyse the standard solutions and apply these to the specific problem which might be solved by one of the standard solutions. Classical TRIZ is a complete toolbox for problem analysis and problem solving. Modern TRIZ is evolved and has many more toolboxes. These TRIZ toolboxes can be deployed within the conceptuation approach for new product development.

40 problem solving (design) principles of TRIZ	
01 Segmentation	21 Skipping
02 Taking out	22 Blessing in disguise
03 Local quality	23 Feedback
04 Asymmetry	24 Intermediary
05 Merging	25 Self-service
06 Universality	26 Copying
07 Russian dolls	27 Cheap short-lived objects
08 Anti-weight	28 Mechanics substitution
09 Preliminary anti-action	29 Pneumatics and hydraulics
10 Preliminary action	30 Flexible shells and thin films
11 Beforehand cushioning	31 Porous materials
12 Equipotentiality	32 Colour changes
13 "The other way round"	33 Homogeneity
14 Spheroidality - Curvature	34 Discarding and recovering
15 Dynamics	35 Parameter changes
16 Partial or excessive actions	36 Phase transitions
17 Another dimension	37 Thermal expansion
18 Mechanical vibration	38 Strong oxidants
19 Periodic action	39 Inert atmosphere
20 Continuity of useful action	40 Composite materials

TRIZ is overcoming barriers by abstracting specific problems into standard problems and its standard problem solving design principles and its subsequent implementation as specific problem solved

5. Perspective

The research group *Transition Bioeconomy* is part of the Research Centre Biobased Economy of the Institute of Life Sciences and Technology of Hanze UAS. Applied research is the main focus of the group within a quadruple helix setting, where science meets business, meets government and meets students. Here, aided by innovation tools like the conceptuation method, new ideas, products and businesses are born, fostering the transition into the circular biobased economy. With the aid of (green) processing and laboratory facilities, new products are created and tested. Interdisciplinary cooperation is prerequisite for achieving biobased goals. The Research Centre Biobased Economy and the Zernike Advance Processing facility offer opportunities for all parties to create a prosperous green future for everyone.



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