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CORDIS Results Pack on

Bio-based innovation

A thematic collection of EU-funded research and innovation results

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Bio-based innovation builds Europe's bioeconomy

Research and Innovation

Contents

Editorial

A global transition from an economy dominated by petrochemical-based processes towards ones that are sustainable, bio-based and circular, is now underway. In this context bio-based innovation has the potential to help to build a bioeconomy that will reduce the European economy's dependence on fossil feedstocks by using CO_2 instead, thereby making a positive contribution to meeting the EU's climate goals, while relieving pressure on ecosystems and helping to create 'green jobs'.

Nature supplies solutions: research pipelines lead the way

Europe's bioeconomy is currently worth EUR 2.2 trillion and employs 18.6 million people across the bloc.

This CORDIS Results Pack highlights 16 EU-funded projects, 4 of which are implemented via the Bio-based industries Joint Undertaking (BBI JU) — a public private partnership of the EU and the Bio-based Industries Consortium (BIC). These projects have considered the use of innovative biological processes and principles — derived from terrestrial and aquatic organisms — for the development of high value applications.

Initiatives, such as BIOOX for example, have developed biological enzymes for the industrial-scale production of chemicals, biopolymers, fragrances and other consumer products in bio-reactors. NewFert used biowaste to produce new green fertilisers. OPTIBIOCAT sifted through the genomes of fungi and bacteria for suitable biocatalysts for use in cosmetics. SmartLi developed technologies for using lignins as raw materials for biomaterials.

SUSY cut the cost of biotechnology processes involving glycosylation by exploiting the unique properties of sugar-modifying enzymes, with applications in the food, chemical, pharmaceutical and personal care industries. PROVIDES employed new natural solvents to improve energy efficiency in the pulp and paper industries.

Latest technologies applied

PUFACHAIN devised a complete procedure using microalgae as a sustainable source of purified polyunsaturated fatty acids for high-value nutrition and pharmaceutical applications. BISIGODOS produced valuable algae-derived chemicals, amino acids and bio-resins for coatings, printing, food, and haircare and adhesive applications.

BIOWAYS increased public awareness of bio-based products and applications. DISCO employed the latest technologies to deliver sustainable bio-sources for high-value plant-derived products. TriForC also built a pipeline to identify and utilise plant-sourced triterpenes, with potential applications in drug design and use in agriculture as biopesticides.

The PROMYS project developed synthetic biology-based platforms fermentation, industrial and pharmaceutical applications. Finally, nature inspired, environmentally friendly, high performance anti-fouling coatings were developed by BYEFOULING for use on ships and marine infrastructure.

Biocatalysts for more eco-friendly chemicals

Bio-oxidation has the potential to overcome the environmental impact of current chemical oxidation processes used for the production of chemicals and intermediates, biopolymers, consumer products, flavours and fragrances.

In the chemical industry, catalysis plays an important role. Most chemicals synthesised industrially use catalysts to speed up the industrial oxidation process or spark it into action. However, chemical oxidations can often result in undesired environmental side effects as they use damaging solvents or toxic compounds. Oxidising materials also pose the risk of explosion or of a highly exothermic reaction.

Involving 11 partners from leading European companies and universities, the EU-funded (BIOOX) project addressed the need to develop new, eco-efficient, and safer manufacturing processes for the chemical industry and end users.

Catalysts from living organisms

Bioprocesses have the potential to overcome the hazardous nature and high environmental impact of current chemical oxidation processes. Harnessing chemical reactions that take place in the cells of living organisms can provide a safer and more eco-friendly way of manufacturing chemicals that delivers high-quality, clean industrial products.

"The aerobic biocatalytic oxidation reactions currently have the potential for the biggest impact on the future uptake of industrial biotechnology in Europe," points out Professor John Whittall. Biocatalysis has long been recognised for its ability to provide a clean, energy-efficient and safe method for oxidative transformations that form the basis of all aerobic life. However, as Prof. Whittall explains, "Biocatalysis reactions have not been widely implemented in the chemical manufacture processes, because of lack of available robust and selective oxidative enzymes."

The aerobic biocatalytic oxidation reactions currently have the potential for the biggest impact on the future uptake of industrial biotechnology in Europe.

The major challenge is that the oxidation environment is damaging to enzymes. Developing, therefore, robust enzymes of

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sufficient activity that can be produced at reasonable costs was the overall objective of BIOOX.

Project advancements

Bio-oxidation is characterised by relatively benign reaction conditions and exquisite selectivity, often realising transformations of precursors which are difficult to produce via traditional chemistry. Project work was geared towards developing advanced tools compared to the state of the art for producing enzymes that synthesise and oxidise alcohols.

New advanced bioinformatics tools enabled researchers to screen the activity of a wide range of different biocatalysts, including oxidases and cytochromes P450s. After selecting diverse enzymes with predicted properties, BIOOX developed an advanced technique termed 'fermenter in a flask' that improves the best enzyme activities and increases their yield from engineered bacterial strains.

Researchers successfully demonstrated the synthesis of hydroxylated fatty acids, alkenes and oxy-functionalised terpenes via cytochrome P450 enzymes. Using alcohol-oxidase enzymes, they also produced aldehydes in high yields. The team then experimented with advanced fermentation methods to produce the desired enzymes at a viable cost. The consortium also scaled up the newly developed reactors — batch and continuous — for evaluation by industry partners.

In general, BIOOX offered new insight into the enzymes and processes that are required to develop new industrial bio-oxidation reactions. "The main focus was to perform oxidation reactions for industrial-scale production of chemicals at a low cost and to boost users' confidence that biocatalysis is not an academic curiosity, but can be transformed in a tool for use in a number of fields," states Prof. Whittall.

Project achievements include technologies for applications in diverse markets, including chemicals and intermediates, biopolymers, consumer products, and flavours and fragrances. The advances made by BIOOX should open the way for biocatalysis to be embraced as a routine technology in the biotechnology industry, also supporting the European knowledge-based bioeconomy.

PROJECT
BIOOX - Developing a validated technology platform for the application of oxygen dependent enzymes in synthesis and transformation of alcohols

COORDINATED BY
University of Manchester, United Kingdom

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
bioox.wpengine.com/

Promoting bio-based products to consumers

A bioeconomy uses renewable resources and helps society meet current environmental challenges, so consumers really need to be made aware of the benefits of bio-based products.

Converting resources from agriculture, forestry, fisheries and aquaculture into food, bio-based products and bio-energy is a promising strategy for minimising our dependency on fossil-based inputs. The bioeconomy has the potential to transform manufacturing processes and industry and reduce their environmental impact. To achieve this, consumers need to be informed about the benefits of bio-based products and its applications.

Promotion activities

The EU-funded BIOWAYS project conducted an EU-wide online survey alongside analysis of relevant studies which helped them to collect qualitative and quantitative data on the public perception on bio-based products. "Our long-term goal is to increase public confidence in the bio-based industry in order to reinforce its market uptake, which in turn will positively impact on society, economy and environment," explains Project Coordinator Iakovos Delioglanis.

The online questionnaire was translated into seven languages and evaluated public perception and engagement with bio-based products, the benefits of utilising them and the reasons that prevent their greater use. Results from over 450 respondents across various EU countries showed that although the majority could identify bio-based products, less than 40 % of the people had sufficient knowledge about them.

Nearly half the respondents lacked information on the benefits of bio-based products while the majority agreed that better labelling and incentives should be offered to consumers. This clearly showed that public awareness needs to be increased through well-targeted and innovative training tools and materials.

Our long-term goal is to increase public confidence in the bio-based industry.

BIOWAYS organised a variety of tailor-made national and international events, including thematic workshops, to engage all stakeholders in an open discussion concerning the future of bio-based products and their environmental, social and economic benefits to European society. During these events, project partners displayed samples of bio-based products and demonstrated how they can be used to create a positive impact on the environment and society. In addition, participants addressed how to overcome bottlenecks to adopting bio-based processes and switching to bio-based products.

The project implemented alternative communication techniques and public engagement activities alongside the development of games, educational tools and fun facts. The communication programme was based on science facts and figures, with well-formulated, understandable and accessible key messages, which outlined the capabilities and benefits of bio-based products. Factsheets were prepared on various bio-based products including packaging, fuels, food ingredients and feed. All this material can be found online.

A step further

The BIOWAYS initiative goes beyond the promotion of bioeconomy. As Delioglanis emphasises: "We set up the Biowatch platform to engage stakeholders, researchers, industry and the general public in an ongoing discussion and sharing of ideas." Biowatch also serves as an electronic library for bio-based research and projects or for anyone interested in the latest developments in bio-based industry and research.

"This online community has the capacity to fuel new research collaborations and increase the opportunities for further funding, leading to scientific discoveries and visibility of the bioeconomy sector," concludes Delioglanis. The BIOWAYS descendant projects BIOBRIDGES and BIOVOICES promise to further increase public awareness and make bio-based products part of everyday life.

PROJECT
BIOWAYS – Increase public awareness of bio-based products and applications supporting the growth of the European bioeconomy

COORDINATED BY
Q-Plan International, Greece

FUNDED UNDER
H2020-BBI-JTI

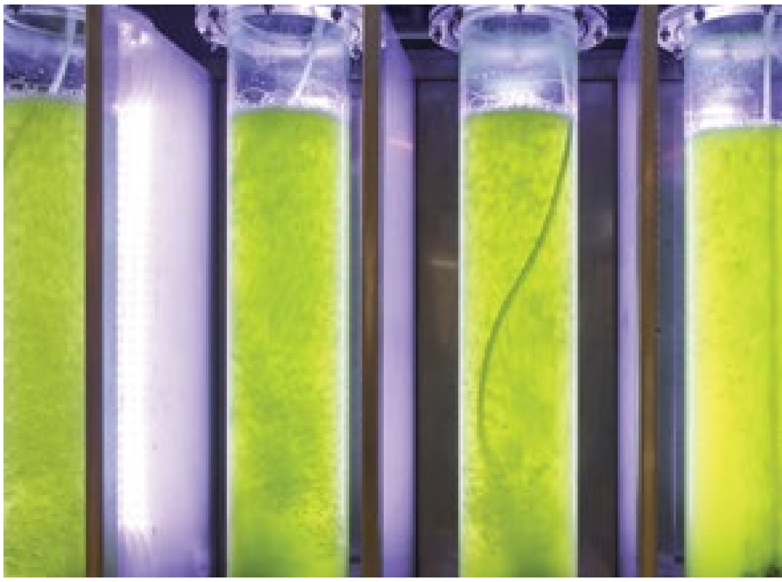
PROJECT WEBSITE
bioways.eu/

Sustainable chemicals from algae

An EU-funded project has successfully built a facility that uses algae to recycle industrial carbon dioxide (CO_2) emissions into valuable chemicals.

Long known for their ability to produce a vast number of different bioactive compounds, microalgae hold great promise for new products in the chemical and pharmaceutical industries as well as the food sector and energy sectors. What's more, algae have rapid growth rates in CO_2 rich environments.

The EU-funded project BISIGODOS, which involves 15 other partners from all over Europe, was established to select and cultivate new varieties of microalgae to facilitate the optimisation of the extraction of products with high added value for industry.



Consuming CO_2 from industry emissions

BISIGODOS is revolutionising how industrial carbon emissions are used. The project succeeded in feeding algae in photobioreactors with CO_2 sourced directly from industrial emissions to ultimately obtain different substances for the production of adhesives, paints and inks. To this end, researchers improved algal strains, redesigned photobioreactors and developed ways to separate and purify algal components.

The challenge of driving down product costs depends on making biomass and downstream processing more cost-competitive in the future.

In the BISIGODOS prototype, marine microalgae efficiently convert CO_2 and sunlight into kilograms of biomass. Researchers then extract lipids from algal cells to be converted into fatty acids. These are used to produce bio-based adhesives and resins for flexible and sustainable packaging.

The remaining fat-free algal cells are then used to produce amino acids for the food and cosmetics industries. Various algae-derived chemicals are also used for anti-corrosive paints, bio-based resins for inks, and compounds for the hair care industry.

Overcoming challenges

One of the most critical issues facing the consortium was to separate algal components from the liquid phase. "The separation process depends on the component physical or chemical properties. Any change in properties such as biomass type, temperature, water content or the catalyst used modifies the product composition and can lead to taking different separation steps," explains Project Coordinator Ana Palanca.

Another decisive aspect was the high costs of the algae-based products compared to those depending on fossil feedstocks. "The significant cost of growing microalgae can stall further development or prove to be a barrier for commercial exploitation of this promising technology. The challenge of driving down product costs depends on making biomass and downstream processing more cost-competitive in the future," points out Palanca.

Although there is a wealth of work still to be done to achieve further progress, algae-based products have revealed significant potential compared to their petrol-based counterparts. For example, algae can be used as an alternative protein source as in addition to the high protein content, they are also rich in vitamins and minerals. Microalgae are also a source of naturally occurring surfactants that are both biodegradable and cheaper.

The appeal of algae is its ability to contribute to greenhouse gas reduction while serving as a feedstock for production of valuable products. BISIGODOS' advanced process effectively transforms microalgae into bio-based chemicals to maximise the value of bio-feedstock and reduce CO_2 waste.

PROJECT
BISIGODOS - High value-added chemicals and BIoreSIns from alGae biorefineries produced from CO_2 provided by industrial emissions

COORDINATED BY
AIMPLAS - Plastics Technology Centre, Spain

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
bisigodos.eu/

New anti-fouling treatments

Researchers have tackled the growth of marine organisms such as barnacles on boat hulls. Unlike previous anti-fouling treatments, the development is low-toxic.

All surfaces in daily contact with seawater water eventually become permanently encrusted with a layer of sedentary marine organisms. Such surfaces include boat hulls, nets, buoys, and other marine infrastructure.

Fouling, as the problem is known, is a serious problem for marine vessels. A heavily fouled boat hull will be very rough and unstreamlined so the vessel will travel more slowly, while also requiring excess engine power. This increases air pollution, plus fuel consumption and other costs.

Left untreated, fouling would eventually render the ship useless. Fouling management is essential but difficult, thereby representing the single largest maintenance cost in shipping.

Conventional anti-fouling paints are generally toxic and may be detrimental to the marine environment. Their toxicity also makes them unsuitable for aquaculture applications.

These properties will reduce ship operating costs and pollution, while also increasing ship lifespans.

Non-toxic coatings from Mother Nature

The EU-funded BYEFOULING project developed environmentally friendly anti-fouling coatings with high performance compared to current options. The new coatings are suitable for large-scale industrial production.

Many marine organisms face the same problem as human boat-owners, but for them preventing the growth of other creatures is a matter of survival. It follows that numerous anti-fouling compounds exist in nature.

A major challenge for BYEFOULING researchers was finding and adapting suitable candidate compounds, which involved detailed study of many marine species and their biochemistries.

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Researchers used various compounds in combination to attack different stages of the fouling process. The team also developed new synthesis methods that could be scaled up. The compounds include protein absorption inhibitors, quorum-sensing inhibitors, and natural biocides. These disrupt specific natural processes by which marine organisms attach to their permanent home, without chemical pollution.

Nano-application

The compounds are applied as paint, which include nanomaterials and their compounds. Certain nanomaterials have intrinsic antifouling properties. Other nanomaterials encapsulate the compounds, while still others contain living organisms for controlled release.

The team developed proof-of-concept demonstrators combining the most promising candidate compounds and nanomaterials. After extensive laboratory testing, researchers conducted field trials in the Mediterranean and Red Seas, plus the Atlantic Ocean. The testing assessed anti-fouling properties and ecotoxicity. Later testing on full-scale models involved demonstrator coatings intended for ships, aquaculture, and buoys. The team also developed special demonstrator products for offshore wind farms.

As researchers hoped, testing demonstrated high anti-fouling performance combined with low toxicity. "These properties will reduce ship operating costs and pollution, while also increasing ship lifespans," says Project Leader Dr Christian Simon.

The same coatings to the aquaculture sector will mean higher growth rates, improved water quality, better control of disease vectors and reduced costs.

Testing and development continues, with the goal of commercialisation for certain applications in the near future. "The market potential is large," explained Dr Simon, "especially for the maritime transport sector."

The team is working on marketing plans, intellectual property protection, and plans for possible further joint ventures. BYEFOULING is also progressing towards gaining international regulative approval for the new coatings.

BYEFOULING's new products will mean improved shipping efficiency, lowered costs, and less polluting exhaust. At the same time, the natural compounds target marine organisms' specific biochemical processes, avoiding generalised toxic impacts. Now that low-toxic anti-fouling agents are available, regulations may eventually require their use.

PROJECT
BYEFOULING – Low-toxic cost-efficient environment-friendly antifouling materials

COORDINATED BY
Stiftelsen Sintef, Norway

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
sintef.no/projectweb/byefouling

Delivering health and wellness products from plants

Bioactive compounds from plant sources are widely used in cosmetics, pharmaceuticals and health supplements. These novel, naturally sourced products are eco-friendly and will improve the quality of life and health of Europeans while contributing directly to the bioeconomy.

The EU-funded DISCO project set out to develop tools and resources for the renewable production of useful chemicals that are typically produced by the chemical industry. Overall, the aim was to "create a framework that can act as a generic pipeline from discovery to industrial valorisation, by employing the very latest enabling technologies to deliver sustainable biosources of plant-derived products," says Project Coordinator Prof. Paul Fraser. The project "represented a timely opportunity to translate innovation into commercial practice."

Sustainable biosources of plant-derived products

DISCO focused on plant-derived natural products that remain the most prolific source of industrially useful compounds known so far. The chemical complexity of these compounds limits industrial production by chemical synthesis because the procedures are often difficult, expensive and detrimental to the environment.

Alternative isolation from natural sources hasn't been straightforward since natural sources are typically low-yielding and limited to a few plant species that aren't particularly responsive to agricultural production processes. Genetic engineering and the exploitation of natural biodiversity offer an alternative approach that will go beyond the present state of the art used to produce beneficial plant products that are traditionally generated by chemical synthesis.

Several classes of high-value natural products with known bioactivity were selected, namely carotenoids, terpenoids and tropane alkaloids. These required the development of new sustainable biosources and greener production chemistries. "A key feature of DISCO was its ability to build on existing and previous EU investments, rapidly and efficiently transferring the tools and strategies developed to new plant-derived target molecules," explains Prof. Fraser.

The aim was to create a framework that can act as a generic pipeline from discovery to industrial valorisation, by employing the very latest enabling technologies to deliver sustainable biosources of plant-derived products.

The bioactive molecules are derived from two important plant families: Solanaceae and Iridaceae. They consist of different plant species and have recently been identified as promising biosources. Team members exploited existing and evolving biodiversity collections of Solanaceae and Iridaceae to perform bioprospecting for known and new bioactive entities and activities.

To understand the plant biosynthetic pathways involved in the formation of high-value plant products, scientists used conventional biochemical approaches together with modern sequencing technologies and strategies. They also employed enabling technologies to facilitate rapid and efficient metabolic engineering and molecular breeding. These technologies enabled the project partners to deliver sustainable biosources of high-value bioactive and industrial phytochemicals.

A key aspect of DISCO was its active dissemination and outreach programme. Peer-reviewed publications and presentations at scientific conferences were complemented by press releases, regional open days, project animations, and interviews with

senior and junior scientists. Training activities contributed to the career prospects of participating trainees and complementary networks within and beyond Europe. It also organised and participated in metabolite training schools. Unique features of the outreach activities included an industrial forum, a workshop and an early-stage researcher session in Chile to ensure outcomes reached the widest audience possible.

Taking plant products from the lab to the market

DISCO contributed to the delivery of the IBR products phytoene and phytofluene into the marketplace. These colourless carotenes are important bioactive ingredients of cosmetics. Beneficial health effects include anti-ageing. Several technical, production and economic feasibility tests with ketocarotenoids demonstrated the potential for superior products that are also significantly (i.e. tenfold) cheaper than current market leaders. "By providing new efficient biosources, DISCO supports the shift from synthetic to biobased production," Prof. Fraser concludes.

PROJECT
DISCO - From DISCOvery to products: A next generation pipeline for the sustainable generation of high-value plant products

COORDINATED BY
Royal Holloway and Bedford New College, United Kingdom

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
disco-fp7.eu/

Perfecting the biotechnological production of chitosans

Researchers with the EU-funded NANO3BIO project are using specially optimised fungi, bacteria and algae to produce the environmentally-friendly chitosans that serve as raw materials for many important applications.

Oil production is slowing, and as a result, renewable resources are becoming increasingly important. In the near future, the biological production of raw materials will have to play an even greater role if we are to meet customer and industry needs in an environmentally friendly manner.

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To help facilitate this transition to the biological production of raw materials, the EU-funded NANO3BIO project has developed a process for the biotechnological production of chitosans.

The huge potential of chitosans

In the biotechnological processes targeted by the NANO3BIO project, specially optimised fungi, bacteria and algae will take over the production of chitosans.

Chitosans can be used as raw materials by the medical, agriculture, water treatment, cosmetics, paper and textile industries, as well as many other applications. For example, one specific chitosan is suitable for finishing seeds to protect them from pests and diseases and to yield richer harvests. Another, acts as an anti-bacterial, film-forming agent in the spray plaster that accelerates scar-free wound healing. In medical applications, specific chitosans can ensure the transport of drugs to their target sites (e.g. in the brain or in cancer cells).

"Chitosans are typically obtained by chemical means from such limited resources as the shells of crabs and shrimps, or rarely, from fungi or squid pens," explains Project Researcher Achim Hennecke. "In the biotechnological processes targeted by the NANO3BIO project, specially optimised fungi, bacteria and algae will take over the production of chitosans."

According to Hennecke, these so-called third-generation chitosans benefit from more defined — or even novel — structural characteristics, clearly defined biological activities and known cellular modes of actions. As a result, they not only create new market opportunities, they are also more efficient, more environmentally friendly and less expensive than using currently available methods.

A menu of important breakthroughs

The NANO3BIO project has already achieved breakthroughs in several critical fields. For example, researchers developed protocols for producing chitosans with better defined structures and a low-cost protein engineering technology to support their biotechnological optimisation. They also successfully isolated and identified the first natural chitosans produced by microalgae.

"The project has identified genes from different organisms that can be used to drive the biotechnological production of chitin and chitosan modifying enzymes," explains Hennecke. "These were then characterised and used for the biotechnological conversion of chitin into new, high-quality chitosans."

For example, NANO3BIO researchers successfully developed electro-spun chitosan nanofibers and electro-sprayed chitosan nanoparticles as technological platforms for the encapsulation and efficient release of bio-actives, vaccines and drugs. They also invented thermo-sensitive chitosan hydrogels, which are promising materials for regenerating damaged tissues.

Another significant outcome of project is its significant insight into the internalisation of chitosan nano-capsules into human cells, a breakthrough that promises targeted delivery of chemotherapeutics to cancer metastases at a very early stage. "This lays the groundwork for the development of more effective therapies with reduced adverse effects and better quality of life for patients," says Hennecke.

According to Hennecke, many of these achievements have huge economic potential. "The NANO3BIO project has achieved encouraging results," he says. "As chitosans are non-toxic, the project has contributed to building an environmentally sustainable European economy and strengthening the competitiveness of European industry and SMEs."

PROJECT
NANO3BIO - NanoBioEngineering of BioInspired BioPolymers

COORDINATED BY
WWU Münster, Germany

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
nano3bio.eu/start/

Green fertilisers from biowaste

Water, food and resource scarcity alongside increasing waste are among the main challenges humanity will face in the years to come. To take advantage of the waste, European researchers have come up with a novel nutrient management solution.

Biowaste — the waste generated from different bio-based sources — accounts for around 20 % of the waste produced in the EU and can serve as a potential resource of valuable chemical compounds, supporting a circular economy. Therefore, biowaste valorisation is considered an alternative, attractive approach in waste management policies.

A new generation of fertilisers

Most fertilisers currently rely heavily on fossil mineral resources for nutrient supply. The idea behind the EU-funded NEWFERT project was to build up an innovative concept for the fertiliser industry that essentially turns ashes of different origins and livestock effluent into a new generation of fertilisers. "Our aim was to develop an industrial fertiliser nutrient recycling scheme that combines fossil with bio-based materials," explains project coordinator and R&D Director of Fertiberia, Javier Brañas.

Researchers identified and analysed more than 45 different types of biowaste from different areas of Europe and selected 10 for introduction into the fertiliser production process, based on their physical and chemical properties. Ashes containing high phosphorous or potassium content and nutrient availability were used directly for fertiliser production. In the case of ashes with insoluble nutrients, NewFert partners developed new biorefining technologies with low input and energy cost to increase nutrient recovery such as phosphate.

Furthermore, to free phosphate minerals (struvite) and nitrogen from pig slurry in a more cost-effective way, the scientists developed a new process. This reduced costs by substitut-

ing the traditional reagent with the action of bacteria that grow naturally in the medium and building a more efficient electrolysis cell for nitrogen recovery. These novel technologies maximised extraction capacity and enabled NewFert partners to obtain appropriate products for the industry. "Collectively, these raw materials allowed us to produce mineral fertilisers at the pilot scale with 15 % of nutrients from biowaste recycling," states Brañas.

Our aim was to develop an industrial fertiliser nutrient recycling scheme that replaces fossil fuel with bio-based materials.

Overall, the project supports Europe's intended transformation towards a sustainable circular economy with resource-efficient production schemes. Implementation of the NewFert technology at European level is expected to reduce raw material dependency and the import of phosphate and potassium. This could mean the reduction of import costs, the improvement of the management of biowaste in a sustainable way through circular economy, and consequently the promotion and diversification of employment in rural communities throughout Europe.

Overcoming obstacles for production of bio-based fertilisers

Contrary to popular misconception, not all biowaste can be used effectively as fertiliser. Suitable biowaste must contain high levels of nutrients available for plant uptake and be free of undesirable components like pathogens, toxins and heavy metals. Additionally, hurdles and bottlenecks affecting transport, logistics and infrastructure in the biomass feedstock supply systems must also be overcome. According to Brañas: "The next generation of fertiliser plants must be built to deal with multiple biomass feedstock in order to produce marketable materials from biowaste." To facilitate this, NewFert created a guide to preliminary acceptance criteria for determining which biowaste can be used as raw material for fertiliser production.

As a next step, Brañas envisages a demonstration project at the European level, involving farmers and biowaste producers in validating the new fertilisers and technology from an agronomic, industrial and economic point of view. "Paramount to the successful commercial deployment of these new green mineral fertilisers is generating consumer confidence," he points out.

PROJECT
NewFert - Nutrient recovery from biobased Waste for Fertilizer production

COORDINATED BY
Fertiberia SA, Spain

FUNDED UNDER
H2020-BBI-JTI

PROJECT WEBSITE
newfert.org/

New enzymes for green cosmetics

The cosmetics industry is in need of more sustainable, eco-friendly and cost-effective technologies. Towards this goal, the OPTIBIOCAT project identified novel enzymes from bacteria and fungi that can produce ingredients with antioxidant activity.

Our aim was to search for new enzymes in fungi and bacteria, with improved and eco-friendly functions.

The chemical synthesis currently employed in the manufacture of cosmetics suffers from limitations such as unwanted side effects and the need for strong chemical conditions. As a result, there is a general consensus towards industrial enzyme-based bioconversions with reduced environmental impact.

The enzymes feruloyl esterases (FAEs) and glucuronoyl esterases (GEs) are traditionally known for their natural capacity to break down lignocellulose, the basis of plant biomass. In addition, they can catalyse the synthesis of a wide range of bioactive molecules with interesting properties, notably antioxidant, with applications in the food, pharmaceuticals and cosmetics industries.

Scientists from the EU-funded OPTIBIOCAT project wished to identify novel enzymes for producing molecules with antioxidant activity for the cosmetics industry. "Our aim was to search for new enzymes in fungi and bacteria with improved and eco-friendly functions," explains Project Coordinator Prof. Vincenza Faraco.

Engineering new enzymes

An impressive portfolio of new enzymes was developed, including more than 550 novel GEs and 500 putative FAEs identified from fungal and bacteria genomes by bioinformatics analyses. Researchers sequenced and annotated the genome of five different yeast species, identifying new FAEs and GEs as well as other enzymes involved in biomass degradation.

OPTIBIOCAT went a step further by designing FAE and GE mutants from new enzymes discovered in the project. The rationale was to improve the efficiency of fermentation/production and stabilise both the enzyme formulations and the life cycle of the biocatalysts. Moreover, starting from three known available FAEs, through random mutagenesis methodology more than 60 000 variants of directed evolution of these enzymes were expressed in yeast. Improved variants with higher operational stability, thermoresistance, yield and productivity were selected using automated workstations.

"These libraries of thousands of enzyme variants represent a source that OPTIBIOCAT partners can further screen for other properties related to applications behind the scope of the project," continues Prof. Faraco. To validate the most promising candidates at industrial scale, scientists produced them in yeast and fungal hosts. Following condition optimisation, production yields of up to 20 litres were achieved.

Expanding the portfolio of antioxidant compounds

At the same time, researchers employed two of the best enzyme candidates to generate and characterise a library of over 300 novel compounds. Amongst the compounds identified were

esters with antioxidant activity, a property that makes these compounds able to add extra value to formulations used in the cosmetics industry. Subsequent *in vitro* testing of some of these compounds for skin irritancy demonstrated their safe profile for use in cosmetics. However, further compound testing is required to validate their potential cosmetic effects.

Overall, the OPTIBIOCAT project improves the synthetic capabilities of FAEs and GEs, concomitantly optimising bioconversion reactions. Importantly, it supports a shift towards enzyme- rather than chemical-based processes that also translates into less animal testing, with obvious socioeconomic implications.

As Prof. Faraco states: "The impact of the study goes beyond the production of cosmetic products containing natural ingredients; knowledge originating from this project is exploitable in future services and/or products in line with the non-academic partners' own development strategies." Considering the multibillion-euro market for industrial enzymes and antioxidants, the deliverables of OPTIBIOCAT will undoubtedly be rapidly commercialised.

PROJECT
OPTIBIOCAT – Optimized esterase biocatalysts for cost-effective industrial production

COORDINATED BY
Universita Degli Studi Di Napoli Ferederico II, Italy

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
optibiocat.eu/

Cutting-edge biotechnology provides new approaches to the production of chemicals and therapeutics

Synthetic biology is an emerging technology that promises to create a new manufacturing paradigm with a clear role in the future bioeconomy. Applications are envisaged in important economic sectors, such as chemistry, medicine, and the environment.

Cell factories are emerging as a promising alternative to produce chemicals and therapeutics in bio-based processes used in industry. However, engineering cells to over-produce target chemicals at high yields and rates conflicts their natural growth rate and poses certain technological challenges.

The EU-funded PROMYS initiative was designed to address the scientific limitations associated with engineering complex biological systems. Traditionally, isolation of high-yield production cell phenotypes requires analysis of large data-sets to identify key genetic components. PROMYS scientists aimed to drastically accelerate the construction, optimisation and performance of cell factories through a novel synthetic biology technology. "We wanted to develop a platform that will help identify better-performing biocatalysts in a high-throughput manner," explains Project Coordinator Prof. Morten Sommer.

Overcoming biotechnology bottlenecks

In fermentation processes, cell factories often show reduced productivity as the overproduction of the target chemical is either toxic or unnecessary. As a result, engineered cells evolve away from the production objective and towards a state of lower production and higher growth rate.

To address this bottleneck, PROMYS generated the so-called 'ligand responsive selection systems', robust biomolecular circuits with integrated sensing modules that sense the cellular state and couple the output to cellular programs. In essence, this poses a non-natural selective pressure on the host cell, with individual cells that don't fulfil production objectives getting destroyed. "In this way the fermentation population can be maintained in the desired state of high productivity, resulting in higher fermentation yields," continues Prof. Sommer.

During the project, researchers had to address scientific issues relating to the development of synthetic pathways, the optimisation of cell factory production, and the control of cell population during fermentation. Towards these goals, they identified specific RNA and protein-based biosensors that could be deployed as ligand responsive selection systems for key metabolites.

We wanted to develop a platform that would help identify better-performing biocatalysts in a high-throughput manner.

Ligand responsive selection was novel to PROMYS and was used instead of standard analytical screening methodologies. "Linking the concentration of a desired chemical with cell survival allowed us to quickly test many biosynthetic pathways, bypassing the time-consuming and highly labour-intensive analytical methods," continues Prof. Sommer.

Through selective cycles of biological optimisation within the synthetic biology framework, researchers managed to optimise specific metabolic processes in engineered cells. At the same time, this allowed them to create numerous cell libraries which were subsequently screened for optimised enzyme function, new synthetic pathways and cell factory optimisation.

Technology applications

Apart from their work on tools and methodology, the project also made significant scientific breakthroughs, providing important insight into the field of synthetic biology. By integrating forward-engineering tools and concepts of synthetic biology, the PROMYS platform helps identify the most advantageous parameters through self-selective cycles of biological optimisation.

Overall, it constitutes a valuable tool in the hands of future chemical engineers, giving them the opportunity to modify cell pathways for the specific objectives of their application. For specific biotechnology applications, it enables the engineering of cell factories for production objectives by overruling the natural inclinations of biological systems.

The project was designed to include industrial partners for product and technology commercialisation. As Prof. Sommer concludes, "The deliverables are expected to have a significant impact on various industrial applications within the chemical industry with multi-million euro revenue potential, including food and beverages, cosmetics and pharmaceuticals."

PROJECT
PROMYS – Programming synthetic networks for bio-based production of value chemicals

COORDINATED BY
Technical University of Denmark, Denmark

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
promys.eu/

New sustainable pulping technologies

The vision of the pulp and paper industry is to significantly reduce carbon dioxide emissions while improving energy and resource efficiency. Hence, a European initiative has developed a breakthrough technology for greener pulp production.

Currently, pulping of wood to isolate cellulose fibres for paper production uses energy-intensive technologies developed more than a century ago — and they require fossil chemicals to work. There is an overall consensus that we should shift towards greener processes that use less energy and are more sustainable, while retaining the efficiency of high-quality pulp production. The pulp and paper industry can make a major contribution towards worldwide resource-efficiency, supporting global efforts to achieve a low-carbon bioeconomy.

Partners of the EU-funded PROVIDES project developed an innovative technology for wood and agro-based lignocellulose raw materials. "Our aim was to achieve 40 % energy reduction and 80 % CO_2 emission reduction in the pulp and papermaking industry," explains Project Coordinator Annita Westenbroek.

Our aim was to achieve 40 % energy reduction and 80 % CO_2 emission reduction in the pulp and papermaking industry.

Deep eutectic solvents

The PROVIDES technology is based on deep eutectic solvents (DESs), a new class of natural solvents. The individual DES components have naturally high melting points above 100° C, but upon mixing they form low-volatility liquids at room temperature.

Discovered 15 years ago, DESs have already been applied in electrochemical applications. "Only 5 years ago it was discovered that some natural DESs show very high lignin solubility, indicating they could be used as novel pulping solvents. In our project we used DESs operating at low temperature and atmospheric pressure to isolate lignin from wood, so that we can obtain pure high-quality cellulose fibres for paper making," continues Westenbroek.

The PROVIDES project developed more than 100 DESs. A few of them demonstrated the unique ability to dissolve and therefore mildly fractionate wood. The generated cellulose fibres were straight and well-shaped, giving rise to paper with good internal bond and tensile strength. The lignin and hemicellulose side streams can be forwarded for further valorisation.

Another significant achievement of the project was the development of the first hydrophobic DESs, which significantly enhanced the isolation of components from aqueous pulp.

Beyond a greener technology

"DES are nature-based, renewable, biodegradable and cost-effective solvents that have never been utilised in the pulp and paper industry or for any other biomass fractionation before," emphasises Westenbroek. Undoubtedly, the discovery of DESs has the potential to revolutionise the pulping process, opening the way to produce pulp with minimal energy, emissions and residues. Importantly, implementation of this radical technology in the paper industry is expected to increase sustainability through energy-, cost- and resource-effectiveness.

Furthermore, DESs could also be used to recover cellulose from waste, and dissolve inks and contaminants in paper for recycling. However, there are many technological gaps that need to be filled to bring this laboratory technology towards the next stage.

Ongoing activities by the PROVIDES consortium aim to optimise the delignification process and improve the recovery and reuse of DESs.

Currently, researchers are preparing for a pilot phase study to test DESs at a higher scale and validate environmental effects and climate benefit. The environmental impact of the PROVIDES project results extend beyond the paper industry, since pure lignin can replace fossil-based aromatics in the chemical sector.

Overall, the PROVIDES approach aims to outperform traditional pulping processes by producing highest quality products at lowest energy consumption and cost. The ultimate goal, Westenbroek concludes, is to "commercially implement the DES technological innovation by 2030 to support the climate goals of the pulp and paper industry."

PROJECT
PROVIDES - PROcesses for Value added fibres by Innovative Deep Eutectic Solvents

COORDINATED BY
Stichting S-ISPT, Netherlands

FUNDED UNDER
H2020-BBI-JTI

PROJECT WEBSITE
providespaper.eu/

Accelerated commercialisation of algae products with pharmaceutical and nutritional potential

European researchers have developed a sustainable source of purified docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). These act as building blocks to create high-value products for nutrition and pharmaceutical applications.

There is a growing market for omega-3 fatty acids, which are polyunsaturated fatty acids (PUFAs). Those most in demand are DHA and EPA, which are present in large amounts of fish oil. However, PUFA exploitation from fish is not sustainable, and the concentration of DHA and EPA in fish oil varies considerably, depending on location, the season and availability of phytoplankton.

Furthermore, there are shortages from overfishing and environmental threats so that the rising demand for PUFAs can no longer be met by fish oil without risking severe damage to or even a collapse of marine organism populations. Microalgae can fill this gap and help to save fish populations and ultimately the marine environment. As a result, they have

emerged as a potential source for EPA and/or DHA. Remarkably, microalgae are the only form of life which can readily produce PUFAs by directly using the sun's energy.

The EU-funded PUFACHAIN project "introduces a sustainable alternative based on microalgae," says Project Coordinator Prof. Dr Thomas Friedl. "We're convinced that the health benefits of PUFAs for consumers are worth the efforts put into algae-based PUFA production." Since PUFAs are valuable components for pharma and food applications, they "provide the potential to make microalgae production economical at an industrial scale," he adds.

Value chain for the industrial development of algae products

Project partners established a value chain from microalgae to PUFAs. Utilising microalgae, they devised a complete procedure from feedstock production and harvesting to oil extraction and purification. Overall, the aim was to further develop a sustainable source of purified DHA and EPA as building blocks towards high-value products for nutrition and pharmaceutical applications.

To create the integrated value chain, scientists began by screening and selecting appropriate algae strains. Then, they further characterised them. Flat panel and tubular photobioreactors were used to develop the most suitable cultivation strategies for both laboratory- and industrial-scale applications.

For the first time, the pharmaceutical and food industries will have a new raw material source from microalgae for high-value products.

An assessment of the value chain's environmental and socioeconomic sustainability was performed to determine which products could potentially go to market. The evaluation helped to identify and optimise drivers of environmental impacts, costs, energy demands and material requirements of certain algae cultivation and extraction processes.

Upscaling the PUFA extraction process

Team members found a sustainable and easy way to extract the valuable fatty acids from the algae biomass while exerting the least energy possible. They examined the effectiveness of different biomass preparation treatments for breaking the algae cell structures and making the released oil available to the extracting solvent.

Two extraction processes were evaluated to produce high-quality oils at lower costs. The first, supercritical fluid extraction, is used to fabricate specialty chemicals for the cosmetic and nutrition industries. It requires CO_2 to collect fatty acid, but needs to dry the biomass before the extraction. The second method uses propane to extract fatty acids from wet algae biomass. By employing purification steps, the team obtained highly purified and concentrated fatty acids from the crude algal oil.

To date, four products have been developed for the pet food market and the nutraceutical and cosmeceutical industries. Another four are on the way. "For the first time, the pharmaceutical and food industries will have a new raw material source from microalgae for high-value products," concludes Prof. Dr Friedl.

PROJECT
PUFACHAIN - The Value Chain from Microalgae to PUFA

COORDINATED BY
Georg August University Göttingen Foundation under Public Law, Germany

FUNDED UNDER
FP7-KBBE

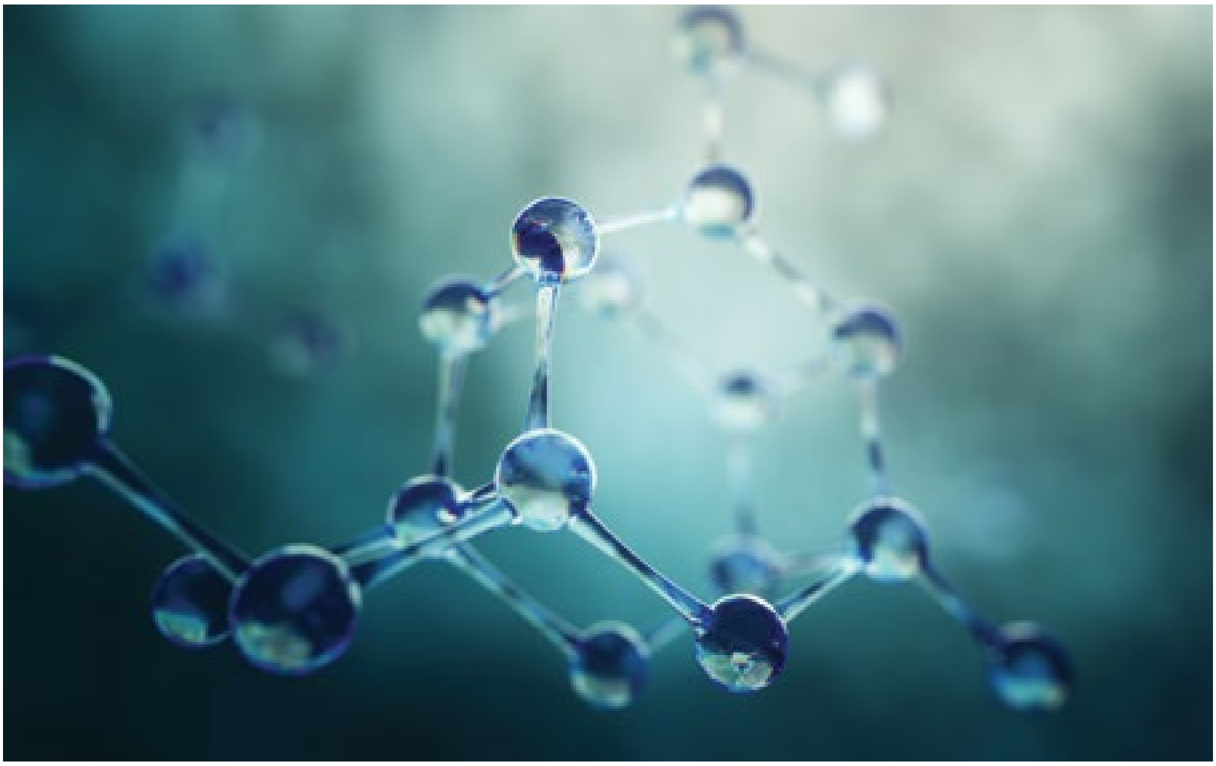
PROJECT WEBSITE
pufachain.eu/home/

Enzyme engineering to boost biotechnology applications

Fusing sugars to small pharmaceutical or food molecules — a process known as glycosylation — can dramatically improve their properties. An EU-funded initiative used advanced enabling biotechnology to develop new, efficient and environmentally friendly processes involving glycosylation.

Glycosylation is a widely used process for improving solubility of healthy food or drug compounds, enhancing the activity of certain antibiotics or modulating the characteristics of flavours or odours. Performing glycosylation reactions via the enzymatic route rather than chemical synthesis is more specific and efficient, environmentally friendly and utilises less energy. However, glycosyltransferases (GTs) — the enzymes that perform the process of glycosylation — require nucleotide-activated sugars to function, which are costly for industrial applications.

The EU-funded SUSY project proposed to address this issue through the development of a more cost-effective multi-step



process based on the unique properties of three types of sugar-modifying enzymes: levansucrase, sucrose synthase and glycosyl transferase. "The idea was to use sucrose as the starting point of the process, which is a very cheap and abundant substrate," notes project coordinator Prof. Tom Desmet. "By combining the three enzymes in a multi-step fashion, we recycle the expensive intermediary compounds throughout the process, reducing considerably the cost of glycosylated products," he explains.

Engineered enzymes with novel properties

Considerable effort went towards addressing certain limitations associated with the natural variants of the employed enzymes, such as narrow specificity and limited stability. In this context, researchers performed extensive molecular engineering to identify new enzyme variants with improved characteristics, including wider substrate specificity. They employed a plethora of expression systems for recombinant expression of the engineered enzymes.

Biocatalysis will constitute a major pillar of the green chemistry, with enzymes offering significant ecological benefits.

In addition, enzyme variants of plant and bacterial origin were identified, and their long-term stability was further increased through co-immobilisation protocols. In particular, the sucrose synthase from *Acidiothiobacillus caldus*, a prokaryotic organism that lives under extreme temperatures, proved the best candidate for engineering purposes. The enzyme was active at elevated temperatures, demonstrating enhanced thermostability as well as promiscuity towards alternative substrates. Effective isolation and downstream processing of the glycosylation products was realised through high-performance liquid chromatography protocols.

Environmentally friendly processes

In the final part of the project the knowledge gained and information obtained was translated to conditions for large-scale glycosylation processes yielding up to 100 g of product. This was performed at pilot-plant facilities of the consortium partners, demonstrating the economic potential of the SUSY technology and supporting subsequent valorisation of project results and technologies. Importantly, researchers evaluated the environmental impact of the newly developed biocatalytic processes, showing that the energy used reduced the ecological footprint of the entire process.

With enzymes serving as important biocatalysts outperforming chemical synthesis, the deliverables of the SUSY project are expected to improve and expand biotechnology applications in the food, chemical, pharmaceutical and personal care industries. The technology has the potential to extend towards galacto-, manno- and fucosylation, broadening the range of synthesised products. At the same time, SUSY will fuel development in the chemical industry by providing the framework for the cost-effective production of glycosides, leading to a whole range of new compounds.

In view of the future, Prof. Desmet envisions that "biocatalysis [will] constitute a major pillar of the green chemistry, with enzymes offering significant ecological benefits, given their low energy consumption and lack of toxic waste generation."

PROJECT
SUSY - Sucrose Synthase as Cost-Effective Mediator of Glycosylation Reactions

COORDINATED BY
Ghent University, Belgium

FUNDED UNDER
FP7-KBBE

Lignin in the chemical industry

Today, nearly all aromatic chemicals are made from oil-based sources. European researchers proposed to use lignin, a structural component of many plants and algae, as an alternative raw material in chemical production.

Lignin is a natural polymer but is available in modified forms as industrial side-streams. The industrial lignins cannot be directly used for the production of biomaterials with acceptable product specifications. Therefore, pre-treatment is necessary to reduce sulfur content and odour, and improve the properties of lignin so that it can be used as reinforcing filler in composites and plasticisers.

The EU-funded SmartLi project developed technologies for ensuring high quality lignin raw materials for manufacturers and industrial end-users. "Apart from industrial feasibility, lignin materials enhance sustainable processes by reducing greenhouse gas emissions as they reduce our dependency on fossil-based materials," explains Project Coordinator Christine Hagström-Näsi.

The project falls under the Bio-Based Industries Joint Undertaking (BBI JU), a EUR 3.7 billion public-private partnership between the EU and the Bio-based Industries Consortium. BBI JU focuses on transforming biological residues and wastes into greener everyday products through innovative technologies. It therefore fosters the transition from a fossil-based economy to a sustainable bio-based economy, generating growth and jobs.

Novel technologies for lignin recovery

Apart from industrial feasibility, lignin materials enhance sustainable processes by reducing greenhouse gas emissions as they reduce our dependency on fossil-based materials.

SmartLi partners developed and tested several protocols for the production of polymeric lignin with improved and constant properties. Using fractionation methods for separating lignin, they were able to recover lignin fractions with equal properties from different starting lignin materials and characterise them. Membrane separation methodologies have also been tested and the lignin fractions analysed in terms of yield, composition and structural features. Furthermore, partners have employed nanofiltration as a non-thermal approach to isolate lignin fractions.

The project successfully demonstrated the antioxidant properties of lignin and its use in the production of thermoplastic polymers. Lignin is also expected to add value to composites by improving their flame retardancy. Importantly, lignin and lignin fractions were evaluated for their potential to replace up to 75 % of phenol in formaldehyde resins. Scientists worked to understand the reactions' mechanisms by employing advanced analytical techniques and assessed the properties of lignin-containing resins in comparison with benchmark industrial recipes.

Lignin-based bioeconomy

SmartLi set out to develop valorisation routes for lignin, sourcing it from pulp and paper industry by-products. The rationale was to support the bioeconomy and replace fossil raw materials, leading to a reduction in greenhouse gas emissions.

Achieving resource efficiency is one of the central objectives of the bioeconomy. To ensure the effectiveness of their innovation process, partners performed sustainability and life-cycle assessment studies as well as techno-economic analyses for the newly developed lignin-based products and technologies. "Performing economic and ecological assessment at an early research stage is central for the development of sustainable processes and products. Our goal was to identify barriers and incentives responsible for market penetration," continues Hagström-Näsi.

Overall, the SmartLi will develop valorisation routes for lignin, bringing new bio-based products to the market and replacing non-renewable resources. The innovative technologies optimised during the project have the potential to be integrated in the current industrial landscape for the production of biomass-based products, creating business opportunities and jobs.

"At the same time, our technologies offer consistent quality to the lignin products, significantly facilitating their uptake into markets," adds Hagström-Näsi. Lignin-based products, which in some cases are even safer than products currently on the market, provide a greener alternative and support the global commitment to building a strong bio-based industrial sector.

PROJECT
SmartLi - Smart Technologies for the Conversion of Industrial Lignins into Sustainable Materials

COORDINATED BY
Clic Innovation OY, Finland

FUNDED UNDER
H2020-BBI-JTI

PROJECT WEBSITE
clicinnovation.fi/projects/smartli/

Functional peptides for next-gen antibiotics

In the face of growing antimicrobial resistance amongst patients, pharmaceutical companies are looking for new compounds. Peptides provide them with thousands of options, but finding suitable candidates is tedious to say the least. An EU-funded project has come up with a method to facilitate their design and production.

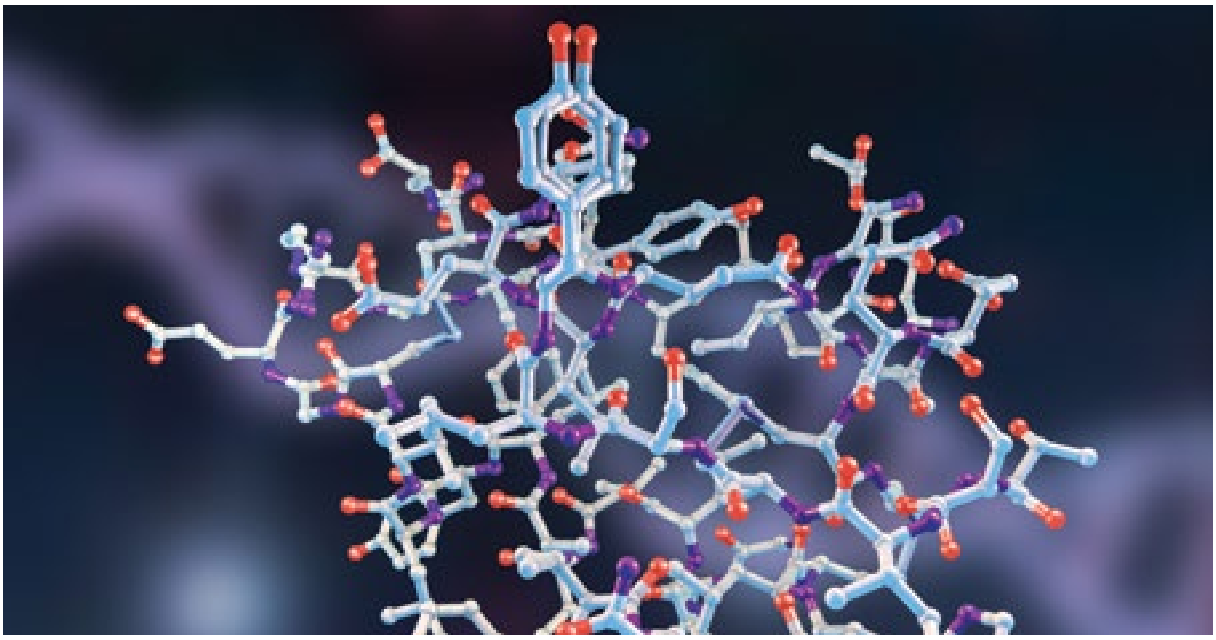
Long considered as a 'no go' area for researchers because of some inherent disadvantages, peptide pharmaceuticals have been booming over the past few years: By 2024, their market value is expected to grow from USD 19.5 to 45.5 million. This success can easily be explained: peptides benefit from greater efficacy, selectivity and specificity than synthetic drugs.

Over 7 000 naturally occurring peptides have been identified so far. The SYNPEPTIDE project aimed to generate variations of peptides with useful function for the pharmaceuticals industry, as well as endow them with new functionalities.

We have found new molecules that show very interesting activities against certain Gram-positive bacteria that are currently a problem in clinics.

"We were looking for novel peptides with antibiotic activity," says Prof. Dr Sven Panke, coordinator of SYNPEPTIDE. "Antibiotic resistance, including multiple antibiotic resistances within the same bacterium, is spreading, so it is important to consider all options to keep treating bacterial infections. Some solutions revolve around optimising our way of administering antibiotics, whilst others focus on finding novel antibiotics. We are following the latter path, by screening bacterial peptide libraries for ideal candidates."

For Prof. Dr Panke and his team, these peptides were the obvious choice to produce the new mol-



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ecules within a reasonable time frame. They focused on a specific group of peptides called lantibiotics — a portmanteau word combining the terms 'lanthionine' and 'antibiotic'. "Lantibiotic-like antibiotic molecules are too complicated for chemists to create rapidly — so we need bacteria to make them," Prof. Dr Panke explains.

The team used a method called directed evolution. They produced myriads of variants of a specific peptide at DNA level, and then inserted this DNA into bacteria. By doing so, they can then use the bacteria to 'read out' the information and translate it into peptide structures.

"We give the DNA to the bacteria, and the bacteria make the peptide," Prof. Dr Panke summarises. "We do it in this way because it is much easier to manipulate DNA than peptides. But the process to get the information from DNA to peptide remains complicated. It requires transcription and translation, ribosomes, tRNAs, etc., and we need living cells for that."

Whereas companies focusing on chemical synthesis can often only create several peptide compounds at a time, SYNPEPTIDE's method allows for production of dozens of thousands of variants.

Once the peptide has been produced, the team can introduce additional functionalities. Standard amino acids are inserted into the peptide, and once ready, the peptide is passed on to so-called post-translational modification enzymes which convert the standard amino acids into the special functions. "We need to make sure that our variants get modified, otherwise they will be not or less active," Prof. Dr Panke points out.

After 4 years of research, the project's strategy works exactly as expected, as Prof. Dr Panke enthuses: "We can produce a broad range of novel peptide variants that get post-translationally modified and are active as antimicrobials. We have found new molecules that show very interesting activities against certain Gram-positive bacteria that are currently a problem in clinics. The next step would be to make more of it, test it in animal experiments, and conduct a variety of tests that show whether they are suitable for use in humans at all. I'd say we are 10 years away from selling them." The consortium is already looking into options to further exploit the project's results.

Until then, SYNPEPTIDE already made a huge step forward by providing leads for a novel class of antibiotics, as well as developing methods to look for them. Prof. Dr Panke hopes that, in this way, the project will eventually have made an important contribution to fighting antibiotic resistance.

PROJECT

SYNPEPTIDE - Synthetic Biology for the production of functional peptides

COORDINATED BY

Swiss Federal Institute of Technology in Zurich, Switzerland

FUNDED UNDER

FP7-KBBE

PROJECT WEBSITE

synpeptide.eu/

Artificial cellular signalling models

Signalling systems allow the cell to perceive its environment and respond accordingly for homeostasis and proper development. Many human diseases, including cancer and diabetes, result from errors in these systems, highlighting the need for powerful tools to study them for development of therapies.

Traditionally, biochemical and molecular biology methods have been used to study cellular signalling pathways, with the focus on individual pathway components alone. However, the advent of omics technologies such as genomics and proteomics alongside systems biology has facilitated a more holistic view on signalling.

To understand the molecular machines implicated in signalling cascades, a detailed view of their architecture and interaction is required. Often, the low endogenous abundance or tissue heterogeneity of certain proteins impedes their extraction, purification and structure elucidation. Scientists often need to resort to recombinant production and purification in heterologous host cell systems. However, this frequently risks compromised, non-physiological behaviour in the specimens studied.

Most medicines marketed by the pharmaceutical industry target signalling cascades to treat diseases. The EU-funded SynSignal consortium took the view that novel tools based on synthetic biology approaches to study new signalling systems could help overcome certain product development challenges.

A synthetic approach to signalling

"Synthetic cellular signalling circuits are perceived as being analogous to electronic circuits," explains project coordinator Dr Imre Berger. "This renders the system accessible for engineering." SynSignal partners designed and engineered individual signalling building blocks and assembled them *in vitro* to produce synthetic cascades that closely resemble the natural processes.

"Each component of the circuit, encoded by a DNA sequence of defined structure and function, is physically interchangeable with compatible modular building blocks," he continues. The tools for DNA assembly and protein production exhibited broad combinatorial potential and could be applied to different types of signalling.

Project members focused on signalling initiated after activation of G-protein-coupled receptors, a large and 'hot' family of membrane proteins that are implicated in many physiological processes including taste and smell. Importantly, these synthetic pathways served as screening platforms for new medicines to treat diseases such as cancer and diabetes. Novel miniaturised bioanalytical methods were also established using mass spectrometry and cryo-electron microscopy.

Mechanistic models and software packages further aided the analysis of signalling pathways and the design of corresponding synthetic signalling circuits that mimicked natural functions. Readout strategies provided unique benefits for molecule discovery, and now pave the way to new flavour, fragrance and nutritional ingredients.

Application of the synthetic signalling toolbox

Overall, the SynSignal project generated innovative synthetic biology platforms and materials to change the way we discover and produce novel products and medicines. "SynSignal platforms will boost the efficiency at which essential signalling pathways that dictate cellular processes can be modified, modulated and interfered with," outlines Dr Berger.

Cost of product development and time required for new products to reach the market will also be reduced. Importantly, this will open entirely new avenues for the development of novel classes of potent and efficient therapeutics and facilitate advances in industrial biotechnology and other multibillion markets.

The open innovation policy pursued in SynSignal allows European pharmaceutical and industrial biotechnology companies to have access to the SynSignal drug discovery technologies. Not only will this accelerate discovery in the life sciences, but it will also provide competitive advantages on a global scale. With signalling systems gaining traction outside of the pharmaceutical industry in the flavour and nutritional industries, for example, the generated tools extend their application beyond biomedical processes. Looking to the future, Dr Berger anticipates "a huge potential for synthetic biology to transform a large number of key areas of important socio-economic challenges, including green technology, drug discovery and manufacturing".

Synthetic biology can be transformational in a large number of key areas of important socioeconomic challenges including green technology and manufacturing.

PROJECT
SynSignal - Synthetic Cellular Signaling Circuits

COORDINATED BY
Swiss Federal Institute of Technology in Lausanne, Switzerland

FUNDED UNDER
FP7-KBBE

PROJECT WEBSITE
synsignal.eu/

Plant-based bioactive compounds for medical and agrochemical applications

A new strategy to identify a specific class of plant compounds — known as triterpenes — aims to help advance science in several ways. New findings appear quite promising for the development and commercialisation of agrochemicals and pharmaceuticals based on those compounds.

Science is continually screening low-molecular-weight compounds from a plethora of synthetic and natural sources in the search for molecules with novel or superior pharmaceutical or biological activities. While plants are a potentially rich source of such molecules, plant metabolism is still under-explored (due to extreme diversity and complex chemistry), and the full potential of plant-derived, low-molecular weight, bioactive compounds is still largely untapped.

Against this background, the EU-funded TriForC project established an innovative strategy for exploiting plant triterpenes, one of the largest classes of plant bioactive compounds, with an astonishing array of structural diversity and spectrum of biological activities. "We have developed a pipeline for the discovery, sustainable production and commercial utilisation of known and novel high-value triterpenes with new or superior biological activities," says Project Coordinator Søren Bak.

Making headway with bioactive triterpenes

Among its key achievements the team identified new bioactive triterpenes for further commercial development of pharmaceuticals and agrochemicals. "The data behind these discoveries are not yet public and one patent has been filed," reveals Mr Bak.

TriForC also established structure-activity relationships of triterpenes, to understand why some triterpenoids have a given biological activity and how this knowledge can be used to develop new drugs or biopesticides for agriculture.

In addition, the project built a genetic toolbox that captures triterpene diversity in the laboratory. "We've identified over 100 enzymatically validated enzyme-encoding genes or regulator-encoding

elements for triterpene metabolic engineering in plants, algae or microbes," explains Mr Bak. The TriForC toolbox has also been used in synthetic biology and combinatorial biochemistry programs to enable custom-designed production of natural and 'new-to-nature' triterpenes.

A closer look at the usefulness of triterpenoids

TriForC, which refers to 'Triterpenes for commercialisation', successfully bridged basic and applied science in this field. It improved understanding of plant secondary metabolism in general, including the synthesis and diversity of triterpenes. Moreover, TriForC set new standards for using plant bioreactors and microalgae in the bioproduction of triterpenoids. The project's research also updated current views of metabolic pathways in plants and how these pathways are structured, activated, and controlled, including how they may have evolved over time.

The TriForC extracts were screened by the partners for their potential in drug design and for use in agriculture such as biopesticides. "We've focused on screening for biologically active triterpenoids with insecticidal and fungicidal potential for agrochemical applications, as well as for drug medicinal targets to treat cancer, inflammation, obesity, diabetes and HIV-1 infection," underlines Mr Bak. "Most of the extracts could be made available for other European researchers," he adds.

We've focused on screening for biologically active triterpenoids with insecticidal and fungicidal potential for agrochemical applications, as well as for drug medicinal targets to treat cancer, inflammation, obesity, diabetes, and HIV-1 infection.

It is interesting to note that triterpenoids are quite often made by plants as defensive compounds to protect specific parts of the plant from being eaten or damaged by insects, bacteria or fungus. Within this context, they often boast very specific and potent biological activities, many of which are exploited already in Chinese herbal remedies or natural oils. "Due to their high structural diversity they are known to have a wide range of commercial applications in the agriculture, food, cosmetics and pharmaceutical sectors, as pesticides, drugs, adjuvants, antimicrobials, anticancer agents, surfactants and preservatives," says Mr Bak.

To ensure long-term continuity of its research efforts, TriForC provided extensive training to early-career scientists through workshops and mentoring, in addition to training participating researchers. It also reached out to broader audiences, especially through the SAW Trust initiative. There is no doubt that the outcomes and dissemination efforts of this project will contribute to valuable new applications and compounds across many fields.

PROJECT

TriForC – A pipeline for the discovery, sustainable production and commercial utilisation of known and novel high-value triterpenes with new or superior biological activities

COORDINATED BY

University of Copenhagen, Denmark

FUNDED UNDER

FP7-KBBE

PROJECT WEBSITE

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RESEARCH*EU MAGAZINE ISSUE 76:
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