

BalticBusiness Quarterly

SPRING 2023



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Pharmacy: Baltic drugs – a good thing?

The Baltic pharma and life sciences industries are rooted in centuries of tradition. Find out what they have to offer today.

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Helping the human body with new technologies

The future trends of the pharmaceutical industry are related to technologies. Pharmaceutical technologies are also the main focus of the Institute of Pharmacy at the University of Tartu.

Ain Raal, Professor of Pharmacognosy at the University of Tartu, agrees that the pharmaceutical industry in Estonia is small, but is growing. “If you look at future trends, they will include nanotechnology”, said Raal. “We study how to make existing materials and substances, whether natural or artificial, receptive to the human body” he added. Raal also sees pharmaceutical technologies as the main direction for the Institute of Pharmacy at the University of Tartu.

A number of achievements

The University of Tartu already has a number of achievements. The 3D printing technology of medicines is being developed at the Institute of Pharmacy, the purpose of which is to prevent, diagnose and treat diseases better. Kristjan Olado, a junior lecturer in pharmaceutical technology at the University of Tartu, said that the production technologies used in the pharmaceutical industry, such as tableting, are not intended for the creation of small-scale personalized drug batches. Therefore, one of the goals of pharmaceutical scientists is to introduce new, more flexible production methods. Laura Viidik, whose doctoral thesis is on the topic of 3D printing of medicines at the University of Tartu, said that in addition to medicines, food supplements are

Pharmaceutical technologies as the main direction for the Institute of Pharmacy at the University of Tartu



also currently being 3D printed. “According to personal needs, a different nutritional supplement is printed in each layer. In this way, one complete tablet is prepared, with a different substance in each layer”, Viidik explained. She added that a similar idea could be implemented in the future so that each tablet layer has a different therapeutic agent. “For a person taking five different medications, for example, it is possible to use 3D printing technology to produce a tablet that contains all of these medical substances.”

Wound treatment of the future

The Institute of Pharmacy of the University of Tartu is also developing technology that would make treating wounds as quick and painless as possible. The wound treatment of the future could be topically administered, long-lasting, antimicrobial and promote normal healing. Kairi Lorenz, a junior lecturer in physical pharmacy at the University of Tartu, who researches wound treatment, points out that chronic non-healing wounds

and ulcers are a big problem that affects approximately 45 million people around the world. According to Lorenz, the wound treatment of the future could be topically administered, i.e. applied directly to the wound, long-lasting, antimicrobial, anti-biofilm and promote normal wound healing. Make medicines smarter

Tambet Teesalu, Professor of nanomedicine, has lately been recognized for the development of messenger peptides that enable the transport of tumour-specific drugs. This will make it possible to use lower drug doses in cancer treatment in the future, which significantly reduces the side effects of drugs. According to Teesalu, only a small part of the administered drugs reaches disease sites, such as tumours, and it is this problem that is being tried to be solved in the laboratory of precision and nanomedicine. “Visually speaking, we’re trying to teach them to distinguish between diseased and normal tissue to increase efficacy and reduce side effects. To do this, we first determine the molecular differences of cancer blood vessels and develop carrier peptides that bind to the blood vessels of the diseased areas. Chemists and materials scientists in our group then attach the peptides to drugs (or nanoparticles loaded with drugs) and the compounds are then tested in disease models”, Teesalu said. According to Raal, most of the pharmaceutical institute’s cooperation projects are in Estonia and Finland, and have not yet reached further abroad. “In financial terms, the projects are of different sizes, some are worth €7,000, others €20,000. There are currently two projects in our institute with funding of over €100,000”, said Raal.

Taltech on the hunt for green medicines

Tallinn University of Technology, or Taltech, does not have a medical or pharmaceutical department, but it has a department of chemistry and biotechnology, whose researchers contribute to the pharmaceutical industry. Recently, their focus has been on the so-called green pharmaceutical industry.

“Today’s pharmaceutical industry is actively looking for solutions to produce new drugs more efficiently and more environmentally friendly. This means both the isolation of bioactive compounds from nature, new synthesis methods, analysis and testing of substances, and improvement. The main force involved in the development of the technology is the chemistry scientists of Tallinn University of Technology, who study both the synthesis of organic compounds and analysis”, said Professor Riina Aav of the Institute of Chemistry and Biotechnology of Tallinn University of Technology. “From this research, we also come into contact with the pharmaceutical industry. Our long cooperation with companies operating in Estonia consists in training specialists with suitable skills at the Institute of Chemistry and Biotechnology, namely our graduates. Both MSc. and PhD graduates are employed in several Estonian chemical companies, such as TBD Pharmatech, which produce and analyze the active ingredients of medicines”, said Cambrex Tallinn, a company that specializes in custom organic synthesis and contract research and development, and has been supporting Taltech chemistry PhD students with scholarships for many years.



TalTech’s research group, led by Professor Riina Aav, contributes to the assessment of the sustainability of synthesis processes

In addition to the Estonian chemical industry, TalTech researchers also participate in several international research consortia. It was at the end of 2022 that the European Union’s green medicines project was launched. Under the leadership of French professor Evelina Colacino, research groups from both Germany and TalTech have participated in the project. In a pilot scheme, the EU-funded project will develop mechanochemical processes to produce several active pharmaceutical ingredients used in drugs. If the concept is proven viable, drug manufacturing would then meet the new environmental stipulations imposed by the EU Green Deal. “Novartis Pharma AG also participates in the same project, where we jointly develop greener methods for the synthesis of active ingredients of drugs using solvent-free mechanochemistry”, said Aav. TalTech’s research group, led by Professor Aav, contributes to the assessment of the sustainability of synthesis processes by analyzing synthesis methods using green metrics and, in the event of detecting dangerous impurities or risks, looks for solutions to make the process safe.

by MĀRIS ĶIRSONS

Photo: Ritvars Skuja



Director of the Latvian Institute of Organic Synthesis, Dr chem. Osvalds Pugovičs: “People always will need drugs, and our scientists have demonstrated their skills by creating new medicines and technologies for synthesising them.”

Latvia's researchers create new drugs

Over 65 years, the Latvian Institute of Organic Synthesis has created 18 new medicinal substances and developed more than 100 production technologies for pharmaceutical products. Currently, the institute is studying the development of new drugs

Director of the Latvian Institute of Organic Synthesis, Dr chem. Osvalds Pugovičs emphasised the fact that the scientific institution has been working since 1957, and currently employs 250 specialists in its laboratories spanning over an area of 5000 m². “Scientists and specialists at the institute have not only created well-known medicinal substances such as tegafur, meldonium, rimantadine, belinostat, but also participated in the development of a new type

of antibiotic,” Pugovičs noted. He proudly highlighted that the Latvian Institute of Organic Synthesis is a leading centre for drug research and innovation in the Baltics, conducting research in pharmacology, molecular biology, organic chemistry, and developing new materials and technologies for the manufacture (synthesis) of various substances. He noted that the net turnover of the institute reached 17.6 million euros in 2022, making it a medium sized company in Latvia. He pointed out that in

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PROF. MAIJA DAMBROVA,
Head of the Laboratory of Pharmaceutical Pharmacology at the Latvian Institute of Organic Synthesis:

“We have the biggest flow of Erasmus students in cooperation with Riga Stradiņš University, who mostly come from Spain and Portugal, but also from the Czech Republic and other countries. Perhaps students from the South want to gain experience in the North and vice versa. The other stream is young Latvians studying abroad and using the grant for an internship in Latvia.”

2022, 58% of the revenue came from the EU, 20% from the USA, about the same amount from Great Britain and Switzerland, and 5% of the business came from Latvia. “About 75% of the institute’s clients have been working with us for more than five years,” Pugovičs said. A new generation of antibiotics “In the mid-nineties, we set up a partnership with the German pharmaceuticals company Merz Pharma, which needed to build a laboratory for drug stability trials, and this partnership has

been around for more than 25 years,” Pugovičs said. IOS’s involvement in an international consortium, established in 2014 with the task of finding a new generation of antibiotics effective against various resistant bacteria, should be mentioned as the most important of the recent partnership projects. “We made applications for a total of 110 ideas, of which 54 were recognised as worthy of development, and 23 of them successfully passed the first round of studies; only 11 passed the next stage, and one drug (apramycin or ELB-1003) is the one for which the first phase of clinical trials was completed in 2020, and which could be very close to getting to pharmacies in the next few years,” Pugovičs said. Involving international scientists The challenge of the next few years will be to implement a European

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EMILIO PARISINI,

Principal Investigator (Head of Biotechnology) at the Latvian Institute of Organic Synthesis in Riga:

“Overall, I feel that the German students who have so far worked in my group were happy with their experience. Likewise, I was happy about their level of motivation as well as their comprehension of the research topics that they worked on. In particular, I feel that what they appreciated the most is the fact that in my lab they could learn to use a wide variety of techniques and experience an interdisciplinary approach to biological problems, rather than having to focus on a single technique or repetitive task.”

research project that has received 2.5 million euros in ERACHair funding. “It is an international project, the goal of which is to research natural substances, which should result in the development of new products,” said Pugovičs, commenting on the latest research project. “Some 20% of the medicinal substances you will see in pharmacy are based on natural substances, so this field of research will become more and more important in the future,” Pugovičs emphasised. “About 20 of our 250 employees are already foreign nationals, and this number will probably increase in the future,” Pugovičs said when asked about attracting foreign specialists. He also hastened to add that OSI gladly accepts chemistry students both from Latvia and from abroad. “There is a lot of competition for brains,” said Pugovičs.

KEY PHARMACEUTICAL DEVELOPMENTS MADE WITH THE PARTICIPATION OF THE LATVIAN INSTITUTE OF ORGANIC SYNTHESIS

APRAMYCIN

ELB-1003 is a next-generation antibiotic developed by the institute, which completed the first phase of clinical trials in 2020.

MELDONIUM

This is a Latvia-invented drug for treatment of the heart and blood vessels, for reducing the amount of energy the heart consumes, and for the general increase of working capacity in healthy people when they face physical stress and are in recovery. One of the creators of meldonium is Ivars Kalviņš, the current president of the Latvian Academy of Sciences.

Meldonium’s registered name is Mildronāts, and it is the most in-demand original product of the pharmaceutical company AS Grindeks.

TEGAFUR

A chemotherapeutic agent for the treatment of various malignant tumours: in particular, stomach, colon, rectal, and breast cancer. Tegafur was first synthesised in December 1964, and a fully-fledged technology for its production was developed two years later. In 1969, tegafur was approved for clinical use in the USSR. Exports of Tegafur to Japan began in 1972 and still continue.

BELINOSTAT

In 2014, the active anti-cancer substance synthesised in Latvia was approved for use in US medical practice in the treatment of peripheral T-cell lymphoma. The active substances were synthesised by Klāra Dikovska, Ivars Kalviņš, and Einārs Loža.

RIMANTADINE

An antiviral product patented by the company DuPont in 1968; Jānis Polis registered an original method for the synthesis of rimantadine in 1969 and conducted a study of its pharmacological profile.



“The Baltic republics have diverse biotech capabilities. Lithuania excels in biotechnology, Latvia in the chemical sector, and Estonia in the academic programs at Tartu University,” Tomas Andrejauskas, the president of the Lithuanian Biotechnology Association

The Lithuanian biotechnology sector has a promising future

by **RUSLANAS IRŽIKEVIČIUS**

The Lithuanian biotechnology sector has a long history extending back two centuries, beginning with the publication of the first biotechnology textbook, *Theory of Living Organisms*, by the renowned professor from Lithuania, Andrius Sniadeckis. The industry has grown steadily over the past 50 years.

An industrial enzyme plant was established in Vilnius fifty years ago, which was followed by the establishment of the Institute of Enzymology and the Life Science Centre at the University of Vilnius. Established seven years ago, the Life Science Centre houses gene-editing technologies. This innovation is now utilized in a wide variety of sectors and applications, including biopharmaceuticals, agrobiotechnology, and environmental applications. Tomas Andrejauskas, the president of the Lithuanian Biotechnology Association, said in an interview with the Baltic Business Quarterly that the industry has grown steadily over the past 50 years, gaining extensive knowledge along the way.

Organic growth

Since a few successful Lithuanian biotechnology businesses were sold for enormous profits, has the biotechnology industry experienced the “Skype effect” of the Estonian IT sector? We asked Mr Andrejauskas. “No, not really”, he responded. In Lithuania, the expansion of the biotechnology industry was not led by a few people, such as Skype in Estonia. Nonetheless, it was the product of the biotechnology knowledge inherited in the form of the Institute of Enzymology when Lithuania regained its independence. Numerous institutes and countless researchers and professors have specialized in life sciences and

biotechnology. It took a long time to build the industry, but once it reached a critical mass, it began to grow organically, and colleges were tasked with filling the need for staff. Some successful enterprises, such as Fermentas, Sicor Biotech and others, were sold to multinational corporations, which contributed to the expansion of the industry. The proprietors of these enterprises allocated a portion of the revenues to the establishment of biotechnology investment funds. “Last year, the Fermentas site, and now the Thermo Fisher Vilnius factory, was the largest Thermo Fisher location outside of the United States and the center of excellence. Last year, it was the largest taxpayer in Lithuania”, claimed Andrejauskas. According to him, we should also bear in mind that the Lithuanian government has earmarked life sciences and biotechnology as one of its top three objectives, followed by public investments. This is due to the fact that the industry requires significantly more investment than other industries, meaning that private investors are ready to take on greater risk provided public funds share the risks. This paradigm is adopted by Lithuania and other nations with significant high-tech industries.

The fastest growing industry

The Lithuanian biotech industry contributes 2.5% to the country's GDP and is seen as a major priority by the government, which hopes to increase its contribution to 5% by 2030. During the pandemic, there was an increase in the market for life science and biotechnological goods, and firms like Thermo Fisher Scientific and Northway Biotech saw robust revenue growth. As a

result, the biotechnology industry in Lithuania surged tenfold over the past decade and became the fastest-growing industry in the nation. The Lithuanian government, scientific institutions, and the business sector are collaborating to achieve a 5% biotech industry contribution to the country's GDP by 2030. According to Andrejauskas, significant efforts have been made to improve the regulatory environment, and expenditures are now being made to aid this objective. Nevertheless, the effort is ongoing, and the association collaborates with the government to identify the necessary investments. The Lithuanian biotech sector's assets include a large talent pool, with 500 students graduating from life science and biotechnology schools annually, a high degree of industry knowledge, and proficiency in gene-editing technologies and proteins for synthetic biology. Andrejauskas commented, “The Life Science Centre at the University of Vilnius, a state-of-the-art facility inaugurated in 2016, is one of the birthplaces of gene-editing technology.” Prof. Šikšnys is one of the four professors responsible for this innovation. Additionally, it is believed that artificial intelligence is becoming a trending subject in the biotechnology business. However, the sector's weakness in Lithuania is the absence of incubators for start-ups and the necessity for accelerator programs.

Regional bases are also included

Furthermore, the biotech sector in Lithuania is not only focused on Vilnius. There are four centres in various cities with diverse

specialties: Vilnius concentrates on medical biotechnology, Kaunas on medical devices and engineering, and Vytautas Magnus University on green/agricultural biotechnology. Additionally, Klaipėda's University is home to a Marine Research Institute for blue biotechnology. The Institute conducts basic and practical research on the marine and coastal environment as well as maritime technology. In addition, the municipality of Panėvžys is focused on industrial biotechnology as a result of the ecosystem formed around the enterprises Roquette Amilina and BioenergyLT. According to Andrejauskas, the Baltic republics have diverse biotech capabilities. Lithuania excels in biotechnology, Latvia in the chemical sector, and Estonia in the academic programs at Tartu University. There is some scientific interaction between the colleges, but there is little business cooperation because the nations are so diverse. Andrejauskas believes that the future of the biotechnology industry in Lithuania is quite promising. The government, scientific institutions, and the business sector are promoting the industry with the aim of achieving a 5% contribution to GDP by 2030. There is an abundance of skill, expertise, fresh university research, and commercial sector investments. In addition, the COVID-19 pandemic demonstrated the need for a local supply chain and the capacity to address unique demands. Andrejauskas further notes that university-based start-ups and spin-offs are expanding significantly. Therefore, the biotech business in Lithuania has a very promising future.