



# Pharmacology in Estonia, Latvia and Lithuania: From historical roots to nowadays achievements



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## ABSTRACT

This Info article offers an overview on the main historical facts and the current perspectives of the scientific and educational competence in field of pharmacology in three European countries on Baltic sea East coast: Estonia, Latvia and Lithuania. The research areas have changed constantly due to economical and political reasons during the last 200 years and today do cover quite different pharmacological areas in each of Baltic countries and are recognized internationally. Today the main topics of studies in Estonia are the pharmacology of neurodegenerative diseases, mood disorders and brain plasticity; the role of mitochondria in neurodegenerative diseases, and the epigenetics of drug dependence. In Latvia, the primary research areas include molecular, neuropharmacology, particularly search for novel medicines capable to halt neurodegenerative diseases as well as cardiovascular pharmacology. In Lithuania the main focus is on clinical pharmacology, rational use of drugs, pharmacoepidemiology and pharmacoecconomy, in experimental pharmacology on regenerative medicine and nephropharmacology. All three countries have their own active Societies of Pharmacology.

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## 1. Introduction

Development of pharmacology in the Baltic area started in two of the oldest Eastern European Universities in Vilnius (transformed from Jesuit College in 1579 by King Stephen Bathory's charter into *Academia et Universitas Vilnensis Societatis Jesu*) and in Tartu (1632 *Academia Gustaviana*).

At that time ecclesiastical education was expanded and physical and natural sciences were introduced by invited world-famous foreign scientists and professors from the West (mainly France, Austria, and Italy) and continued by locally educated pharmacologists. The pharmacology in Estonia, at the University of Tartu as a separate discipline began to flourish in the 19th century and it has become the place of birth of experimental pharmacology as scientific subject. In Latvia the Faculty of Medicine with teaching of Pharmacology was started in 1919 when the University of Latvia was founded. The constant changes in national independence and governance of all three Baltic countries during the last hundred years have resulted in growth and decline, closures and revival of educational and scientific activities of pharmacology in all three countries.

## 2. Pharmacology in Estonia

### 2.1. Before 1918

Although medicine has been taught at the University since the foundation of its ancestor, *Academia Dorpatensis (Academia Gusta-*

*viana*), in 1632, and a separated course on drug names has been part of the curricula since 1689, medicine and its separate disciplines, including pharmacology, began to flourish in the 19th century. That century in medicine and pharmacology in Tartu could be described by a long list of its famous professors (Karl Ernst von Baer, Alexander Schmidt etc.), and by a number of ground-breaking discoveries that remain valid today.

In April 1802, under governance of the Russian Emperor and support of Baltic-German elite the University was reopened in Dorpat (today: Tartu) as the *Kaiserliche Universität zu Dorpat*.

The Medical Faculty was one of the four faculties opened in 1802. It had six institutes, including the Institute of *Materia medica*, Dietetics and History of Medicine. In 1865, the institute was renamed The Institute of Pharmacology, Dietetics and History of Medicine, which was changed to the Institute of Pharmacology at the beginning of the 20th century [1].

The first Professor of the Institute (from 1802 to 1826) was Martin Ernst Styx (1759–1829), although Professor of Medicine, he gave lectures on *materia medica* presenting medicinal substances and herbal drugs in alphabetical order. However, his impact on medicine and healthcare was far more important by lecturing and popularizing hygiene. Theoretical teaching of *materia medica* was rendered more illustrative in 1829 by Johann Friedrich von Erdmann (1778–1846). On his initiative, a large collection of drugs and herbs was collected for teaching [2].

Until the middle of the 19th century, encyclopedism was the model of teaching. *Materia medica* was taught based on earlier



**Fig. 1.** Rudolf Buchheim (from Archive of the Department of Pharmacology).

practices but there was no chemical analysis of the substances or experimental investigation of their effects.

Professor Friedrich Oesterlen (1812–1877) was Chair of the Institute for a short time (1846–1847) and afterwards led the Institute of Therapy and Clinic. In his handbook of drugs (*Handbuch der Heilmittellehre*, published: 1844), he emphasised the necessity to study drugs experimentally. This idea could be seen as step towards changing pharmacology as a discipline [1,2].

Pharmacology as a separate science emerged in 1847 when Rudolf Buchheim (1820–1879, Fig. 1) was appointed as Chair of the Institute. As there was no outside funding, Buchheim built a laboratory at his own expense in the basement of his home (in 1848, the first works based on the experiments made there were published) [2]. Due to his action, Tartu became the birthplace of *Experimental Pharmacology*.

Buchheim's reputation is overshadowed by that of his student and assistant, Johann Ernst Oswald Schmiedeberg (1838–1921). Schmiedeberg's early studies in Tartu focussed on the pharmacology of chloroform and chloral hydrate but his international reputation came from his studies on the alkaloid muscarine. In 1869, Schmiedeberg and his assistant Koppe showed that muscarine evoked the same effect on the heart as electrical stimulation of the vagus nerve, an effect that was inhibited by atropine. This work could be considered the basis for the pharmacology of the autonomic (vegetative) nervous system [1,2]. In 1872, he was invited to Germany to be the Chair of the Institute of Pharmacology in the newly opened University of Strasbourg. Later, most of pharmacology professors in Germany and several other countries including Estonia were the men Schmiedeberg had trained during his 46 years in Strassbourg [1,2].

Next professor of Pharmacology in Tartu was Rudolf Boehm (1844–1926), who is most important studies were on the effects of arsenic on blood vessels. Hans Horst Meyer (1853–1939), Institute Chair from 1882 to 1884, studied the relationship between lipophilicity and potency of general anaesthetics. He observed that lipophilicity is an essential factor in the efficacy of anaesthetics, and published his findings almost two years before C.E. Overton [2]. This theory remains valid today and is known as the Meyer-Overton hypothesis.

The next Chair of the Institute, Schmiedeberg's student, Rudolf Kobert (1854–1918), demonstrated the calming effect of scopo-

lamine, which led to its use in psychiatry. Although he concentrated more on toxicology, he tried to build a bridge between experimental and clinical pharmacology. In 1896, he published a textbook of pharmacology where the administration of drugs for curative purposes was called *pharmacotherapy* for the first time.

In the wave of Russification in 1890s, Russian was introduced as the language of instruction at the University and Kobert had to leave [1]. In 1897, the Lithuanian professor Stanislav Czirwinski (1852–1922), from Moscow University, continued the work of his predecessors including study of the vagal control of heart rate and blood-pressure. He later founded his own Experimental Pharmacology lineage in Moscow [2]. The last long-term Chair of Pharmacology before independent Estonia was David Lavrov (1867–1929).

## 2.2. Independent Estonia

Estonia declared its independence on 24th February 1918. In December 1919, the University was reopened, now in the Republic of Estonia, under the name of the University of Tartu using Estonian as the language of instruction. In the years until Soviet occupation, research in pharmacology focussed mainly on the following areas: sex hormones (Loewe), the pharmacology of the hematopoietic system and analgesics (Barkan and Kingisepp).

In 1921, Siegfried Loewe (1884–1963) became Chair of the Institute of Pharmacology. During his eight years in Tartu, he led efforts to develop methods of quantitative analysis in pharmacology. The bologram method to evaluate drug-drug interactions, built in collaboration with Muischnek, is world-famous [2]. His successor, Professor Georg Barkan (1889–1945) conducted many studies to understand the basic physiologic mechanisms of the human body. His most interesting findings were on bilirubin and haemoglobin in blood [1,2]. In 1938, the first Estonian professor of pharmacology, Georg Kingisepp (1889–1974), became Chair of the Institute.

Although the University of Tartu was opened as an Estonian university, the lack of Estonian-speaking professors resulted in situation, where professors of pharmacology were invited from abroad and Pharmacology was not taught in Estonian until 1930, when docent Elise Käer-Kingisepp began lecturing.

## 2.3. Soviet period (1944–1991)

During the period of Soviet Union rule in Estonia, experimental work and teaching in Estonian at the University of Tartu, continued. Professor Kingisepp continued as the Chair of the Institute until 1972. The most important pharmacological studies from 1930s to mid-1960s of Professor Kingisepp and his students (Olaf Rajavee, Elmar Vasar, Hilja Kurvits and Leo Nurmand) were on cardiac glycosides, sex hormones, analgesics and sedatives. Several new active substances were brought to clinic: vipraxin, viprosal, sulfo-camphocaine etc. In 1968, the Laboratory of Psychopharmacology, that brought together scientists from Institutes of Pharmacology, Psychiatry and Biochemistry, was formed [1]. Laboratory was successful and during the following decades line of scientists (who became professors of pharmacology or other nearby fields later) such as Leo Nurmand, Lembit Allikmets, Alexander Zharkovsky, Eero Vasar, Lembit Rägo, Jaanus Harro etc., defended their thesis in pharmacology.

From 1970s, direction in pharmacological research has been neuropharmacology. In 1972, Professor Lembit Allikmets became Chair of the Institute of Pharmacology. Under his leadership, the Institute focussed on experimental psychopharmacology. The mechanism of action of several neurotrophic and psychotropic substances was studied. The clarification of the pharmacology and toxicology of new GABA derivatives and bringing them to clinical practice, and showing the role of serotonergic system in the mech-

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