

pharma
waldhof

a member of the ACETO group

Nucleotides & Nucleosides

Where we are, where we go.

Antivirals

Antimetabolites

Cardiovasculars

Hepatoprotectors

Vasodilators

biochemicals

chemicals

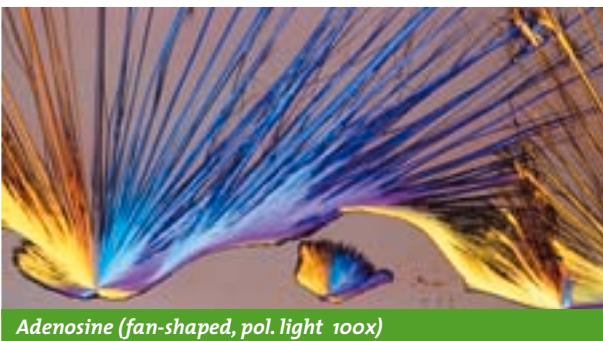
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1947 2004

Your Partner in Nucleic Acid Biochemistry since 1947

1974



Nucleic Acid Biochemistry

– a brief general outline –

Since science became interested in elucidating biochemical interactions and processes in living cells, extensive investigations of chemical structures, biosynthesis and metabolic regulations of the biopolymers RNA and DNA (Ribonucleic acid and Deoxyribonucleic acid), belonging to the most important components of living cells, viruses and plasmids, preoccupied a large part of biochemical research work all over the world.

During the past decades biochemistry and medicine faced a booming development. In this connection, the elucidation of the mechanisms of action of RNA and DNA and, in particular, of their natural and chemically modified components, as well as the search for new fields of application, e.g. in medicine and closely related fields, still remain in the forefront of medical and biochemical interest. The systematic development of new biologically active substances, based on RNA & DNA biochemistry, highly interesting and involving not only biochemists but also human geneticists, microbiologists and physicians, is steadily gaining value and importance. This development is also documented by the immense amount of scientific publications, by the large number of research reagents and active ingredients for pharmaceutical, diagnostic, cosmetic, nutraceutical and further applications which have been developed and put on the market during the last 30 years.

*It is well known that RNA and DNA play a key role as to the regulation of protein biosynthesis in the metabolism of living cells. RNA and DNA have essential structural similarities but are different in their functions. DNA stores genetic information which, by means of identical replication of the DNA molecules in the process of cell fractionation, is transferred to the daughter cells. RNA mainly serves the transcription of genetic information from the DNA and its expression in the living cells. There is a large number of natural, chemically or enzymatically modified RNA and DNA components (**Nucleotides & Nucleosides** and their analogues) interfering with the cytokinesis. Many of them are successfully applied in the modern chemotherapy, e.g. in the treatment of viral infections of different kinds and origins, of pathologically caused cell mutations (malignant diseases), of specific cardiovascular insufficiencies and of metabolic disorders, just only to mention some of the major therapeutic fields being already in the focus of scientific and public attention.*

2006

The Biochemistry at Pharma Waldhof

Who we are – a brief abstract of our background and activities

It started in 1947 already...

Ever since its first technical developments in 1947, our company, legally independent since 1974, has devoted itself over more than five decades to the scientifically most interesting and forward-looking field of **Nucleic acid biochemistry**. However, we started our proper business activities soon afterwards, establishing for the first time ever in the world the manufacture of **Ribonucleic acids** (from yeast) and of its natural components (**Ribonucleosides/Nucleotides**) on a semi-industrial scale.

More than 50 years of know how and expertise – basic elements for our future ...

Today we are somewhat proud to refer to more than 50 years of practical experience in the unique world of **Nucleic acid biochemistry** being a sound basis and highly motivating us for the future. Our domain is the development and commercialization of active substances, key intermediates and reagents for multiple applications in pharmaceuticals, diagnostics, cosmetics and nutraceuticals, in molecular biology and in medical and biochemical research as well, just only to mention the most important business fields.

Nucleosides & Nucleotides – for today and for tomorrow ...

Within the past decades, **Pharma Waldhof** has pioneered a great number of chemical and enzymatic manufacturing processes for **Nucleotides** and **Nucleosides** and their analogues as well. Nowadays, we are focused on new fields of application in pharmacy, biochemistry and biotechnology, on the search for innovative manufacturing technologies for new molecules which may step into the forefront of medical research and development and of closely related fields as well. This constantly means new challenges for us. We test our skills on the achievement of our targets and on the acceptance of the market.

Who we are – a brief abstract of our background and activities

New developments are our strengths ...

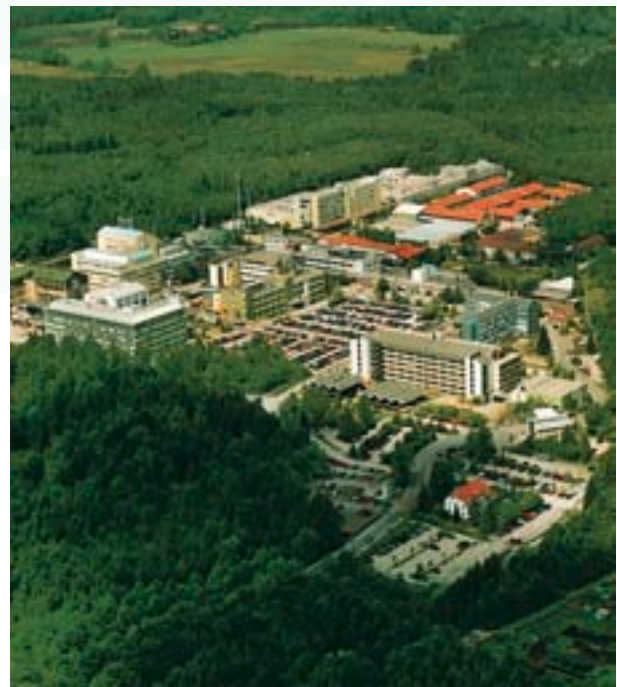
Hence it follows that we are taking a particular interest in new product developments and advanced manufacturing techniques for antiviral, cancerostatic and cardiovascular drug substances and for their key intermediates as well. It is in the nature of our activities that we put our main emphasis on **Nucleotides**, **Nucleosides** and their analogues. For **Pharma Waldhof** innovation, however, also means to steadily improve the traditionally high and recognized quality standard of its products and services. It is our aim not only to meet the growing requirements of the market and the regulatory conditions but rather to establish new standards at high level.



Roche Diagnostics GmbH (plant Mannheim-Waldhof, Germany) former parent company where Active Pharmaceutical Ingredients are manufactured and further services performed for and on behalf of Pharma Waldhof

Our environment – our skills, our ambitions ...

The current range of biochemicals **Pharma Waldhof** roughly comprises 200 compounds enjoying regular scientific and commercial interest. Our new affiliation (since 2004) to the multinational ACETO group of companies, headquartered in the U.S., and our continued manufacturing and technical collaboration with Roche Diagnostics, Germany, our former parent company, and further cooperations with selected biotechnology companies and research institutions as well qualify us to flexibly respond to specific demands and developments in biochemistry and biotechnology, in pharmacy and diagnostics, in cosmetology and in nutrition physiology of today and tomorrow.



Roche Diagnostics GmbH (plant Penzberg/Upper Bavaria, Germany) manufacturing site of various nucleotides, coenzymes and carbohydrates, being developed for and/or just co-marketed by Pharma Waldhof

Know how and Technology

...where Chemistry meets Biotechnology

*Thanks to its experiences of many years in product development and biochemical manufacture, and due to its continued manufacturing and technical collaboration with Roche Diagnostics, Germany, its former parent company, **Pharma Waldhof** disposes of particular know how and has access to virtually every kind of common organic and enzymatic reactions and to bioconversions as well.*

*The ongoing technical partnership with Roche Diagnostics and, in addition, cooperations with other selected biochemical companies around the world offer **Pharma Waldhof** a wide range of manufacturing and process development facilities for active ingredients, key intermediates and reagents from small laboratory and typical pilot to large commercial scale.*

Needless to add that all manufacturing units for drug substances and key intermediates meet the current national and supranational regulatory requirements, i.e. comply with the current GMP standards, with ICH Q7A and other EU or German guidelines and regulations, and are regularly inspected by both the US Food & Drug Administration and the competent German authorities.



Roche Diagnostics GmbH, Mannheim, Germany



Roche Diagnostics GmbH, Mannheim, Germany

Conception and Philosophy

Custom Manufacturing and Product Development

- Experiences of many years in product development and manufacture of Specialty biochemicals
- Scientific know how and biochemical expertise
- Innovative technologies in collaboration with selected industrial partners and advanced research institutions
- “State-of-the-Art” manufacturing facilities, quality assurance and regulatory competence in place at Roche Diagnostics, Germany, our former parent company
- Efficient sales & marketing structures with particular customer orientation, connected with the unique global distribution network of the ACETO Corporation, USA, our new parent company,

enable **Pharma Waldhof** to offer products, conceptions and services being designed for the needs of modern biochemistry, diagnostics and pharmacy, cosmetics & beauty care and functional nutrition as well.

The commercial and logistic infrastructure and the techno-scientific expertise within **Pharma Waldhof** and its partners put us in the position not only to keep but rather to improve the high standard of our products and, moreover, to provide individual services and solutions for our valued customers such as

- customized product and/or process development of new molecules and up-scaling to commercial order manufacturing
- design of specific analytical parameters and methods, compiling of material safety data
- compliance with particular chemo-physical product requirements and/or quality standards
- answering regulatory questions, preparation of Drug Master Files or similar documentations to support product registrations such as IND, NDA, MAA (EU) etc. or other regulatory requirements.



Trifluridine (flowers, pol. light 100x)

Main Product Groups

...and typical molecules belonging to

Arabinonucleosides and phosphates

- ▶ Cytarabine (Ara-C), Fludarabine phosphate, Vidarabine (Ara-A), Vidarabine phosphate (Ara-AMP), Uracilarabinoside (Ara-U)...

Carbohydrates (Monosaccharides, Sugar Nucleotides)

- ▶ Acetyltribenzoylribose, D-Ribose, Deoxy-D-Ribose, Glucose-6-phosphate, GDP-Mannose, UDP-N-Acetylglucosamine, UDP-Galactose, UDPG...

Coenzymes and Cofactors

- ▶ Coenzyme A (CoA), NAD (DPN), NADH (DPNH), NADP (TPN), NADPH (TNPH)...

Cyclophosphates (cyclic Ribonucleotides)

- ▶ cyclic AMP, Dibutyryl-cyclic AMP (Bucladesine), cyclic GMP...

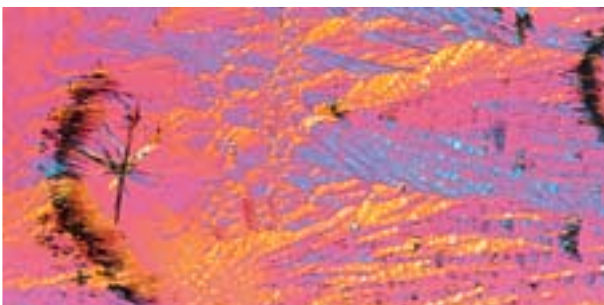
Deoxynucleic acids (DNA) and salts

Deoxynucleosides and analogues

- ▶ Brivudine (BVDU), Broxuridine (BrDU), dAdenosine, dCytidine, dGuanosine, dUridine, Floxuridine (FUDR), Ibacitabine (IDC), Idoxuridine (IDU), Thymidine, Trifluridine (F₃TDR)...

Deoxynucleotides (Mono- and Triphosphates)

- ▶ dAMP, dCMP, dGMP, TMP, dATP, dCTP, dGTP...



Didanosine (scale structure, pol. light 50x)

Dideoxynucleosides

- ▶ Didanosine (DDI), Stavudine (D₄T), Zalcitabine (DDC), Zidovudine (AZT)...

Dideoxynucleotides (Triphosphates)

- ▶ ddATP, ddCTP, ddGTP...

Purines and Pyrimidines

- ▶ Adenine, Benzyladenine, Chloroguanine, Cytosine, Dichloropurine, Fluorouracil, Iodouracil, Kinetine, Mercaptopurine, Thioguanine, Thymine, Xanthine...

Ribonucleic acids (RNA) and salts

Ribonucleosides and analogues

- ▶ Adenosine, 2-Chloroadenosine, Cytidine, Fluorouridine, Guanosine, Inosine, Thioguanosine, Tosyladenosine, Triacetyluridine, Uridine, Xanthosine...

Ribonucleotides (Mono-, Di- and Triphosphates)

- ▶ ADP, AMP, ATP, CDP, Citicoline, CMP, CTP, GDP, GTP, IMP, UDP, UMP, UTP and Thiophosphates...

Miscellaneous compounds

- ▶ Ademethionine (SAME), Creatine phosphate, Glutathione, red. (GSH) and Glutathione, oxid. (GSSG)



1947

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Your partner in Nucleic Acid Biochemistry since 1947

1974

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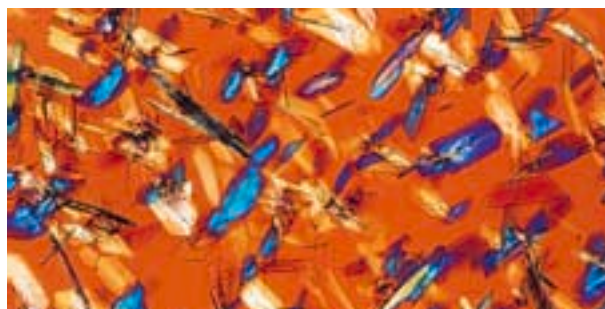
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2004
**Expertise and Competence in
Nucleosides & Nucleotides for more than 50 years**

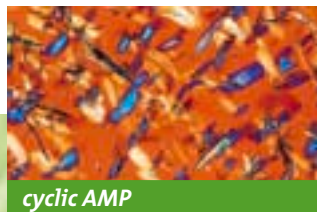
2006



cyclic AMP (flying crystals, pol. light 200x)

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Active Substances (APIs)

Diagnostics

Nutraceuticals

Reagents for R&D

Key Intermediates

bioche