

New effective prodrug strategies

The innovation

The platform technology presented here focuses on new effective prodrugs of amidines and guanidines which are less basic, better soluble, and are absorbed from the gastrointestinal tract.

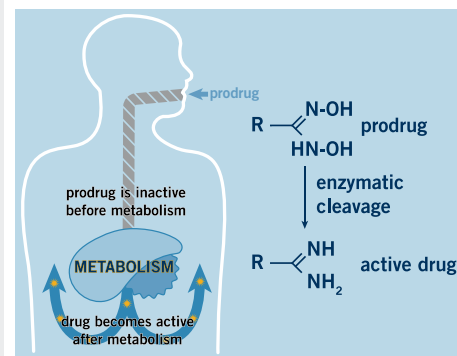
The clinical development of new drugs is often terminated due to unfavorable pharmacokinetic characteristics, such as poor bioavailability of the drug after oral administration or inadequate blood-brain barrier permeability. Prodrugs – in a broad sense – are defined as therapeutic agents which are pharmacologically inactive but are transformed into active metabolites. Compared to other state-of-the-art prodrug approaches, the technology presented here will lead to new derivatives with both better solubilities as well as improved gastrointestinal absorption. Due to their improved stability, the undesired release of activated drugs within the gastrointestinal tract from these new prodrugs should be lower than from other known amidine or guanidine prodrugs. Pharmacokinetic studies clearly indicate that the prodrugs presented here are physiologically metabolised to the active drug after absorption from the gastrointestinal tract. One additional focus of the

technology presented here is the development of amidine and guanidine prodrugs which efficiently cross the blood-brain barrier and release the active drug in the cerebrospinal fluid and the brain.

Amidines and guanidines are components of several marketed drugs as well as promising drug candidates belonging to the groups of:

- trypanocidal and leishmanicidal drugs and actives against *Pneumocystis carinii*
- thrombin inhibitors or factor Xa inhibitors
- glycoprotein IIb-IIIa antagonists
- antiviral drugs (e.g. neuraminidase inhibitors)

While many of these drugs may be inhaled or administered by injection due to their low oral bioavailability, the presented platform technology will lead to prodrugs that could be applied orally. Consequently, the application of the presented prodrug technology will result in cost savings, safety increase and enhanced patient compliance.



Advantages at a glance

- Universal prodrug technology applicable for various drugs
- Simultaneous enhancement of membrane permeability and solubility
- Improved blood-brain barrier transportation
- Reduced undesired activation of drugs within the gastrointestinal tract
- Strategies for the preparative synthesis of various prodrugs established
- Sufficient amounts of selected model prodrugs available
- Hybrid Abridged Applications according to Directive 2001/83/EC Art. 10(3) possible

Keywords

- Improved oral bioavailability
- Blood-brain barrier transportation
- Universal prodrug technology
- Amidine or guanidine functions
- Antivirals
- Antiseptics
- Anticoagulants & Thrombolytics

Areas of application

- Widely applicable prodrug concept to overcome pharmacokinetic barriers
- Preparation of orally applicable drugs
- Antiviral, thrombolytic, anticoagulant or antiseptic actives
- Applicable for already marketed drugs as well as candidates in development

Patent status

The invention is covered by patent families, which are filed internationally and owned by Dritte Patentportfolio Beteiligungsgesellschaft mbH & Co. KG. The first application was filed in July 2006.

To acquire a licence for this new technology, please don't hesitate to contact us!



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