

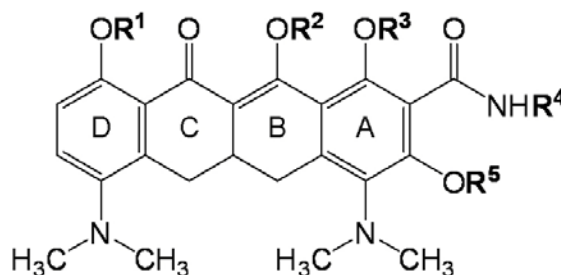
Method for the Synthesis of A-Ring-Aromatized Acetyl-Minocyclines

Background

The tetracycline derivative minocycline is clinically used as antibiotic and for the treatment of inflammatory diseases (e.g. rheumatoid arthritis). Recently, also neuroprotective and cytoprotective properties of this drug have been reported in various models such as Parkinson's diseases, Alzheimer's disease, ischemia, amyotrophic lateral sclerosis, traumatic brain injury, Huntington's disease, spinal cord injury, and multiple sclerosis. As minocycline has long been proven to be safe and to effectively cross the blood-brain barrier, it is currently under clinical investigation of several neurodegenerative diseases. However, high dosages of this antibiotic are needed and the routinely or precautionary application will raise further problems such as bacterial resistance.

The technology

The aim was to improve the pharmacokinetics of minocycline (e.g. "prodrug"-concept) in combination with the elimination of the antibiotic activity. The claimed method is a process for the synthesis and the purification of such derivatives of minocycline. A-ring-aromatized single and multi acetylated derivatives are synthesized in a one-step reaction (Figure). The procedure of an acetylation (R^1 to R^5 in the Figure) is linked with the aromatization of the A-ring of the tetracycline. The purified substances (Tetra- and Pentaacetylcyclin) exhibit a similar neuroprotective potential as minocycline, but surprisingly at much lower concentrations, as tested in our cell culture model. Additionally, these compounds do not possess antibiotic activity against *E. coli*. The obtained semi-synthetic substances are promising candidates for further neuro- and cytoprotective drug development.



Commercialization

We are seeking to establish collaboration and licensing relationships to develop this exciting technology.

Patent status

For this technology a German Patent Application and a PCT Application were filed.

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