Flavi-Block – a pan-flavivirus inhibitor

Low-molecular weight compounds for prevention or treatment of Flavivirus infections including Yellow Fever, Dengue virus, West-Nile-virus, Zika virus and others.

- Broad antiviral activity against RNA virus like HCV, DENV but also to Zika virus, West-Nile virus, Yellow Fever virus, Kunjin virus, Tick-borne encephalitis virus, Japanese encephalities virus, Staint Louis encephalitis virus
- Superior antiviral activity
- No cytotoxicity
- Long plasma stability

Fields of application

Medicinal products for the prevention or treatment of infections with RNA viruses, in particular viruses from the Flaviviridae family, which cause several diseases requiring very high levels of medical treatment or where no therapy is available.

Background

RNA viruses are responsible for numerous serious diseases such as Measles or Ebola. A highly relevant group of RNA-viruses with numerous members is the family of Flaviviridae. This family include viruses of human pathological relevance, such as Hepatitis C virus (HCV) which infects 150 to 200 milion people per year worldwide or the emerging Dengue virus (DENV) with estimated 390 million infections per year.

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Service
Technologie-Lizenz-Büro GmbH has been entrusted with exploiting this technology and assisting companies in obtaining licenses.

Problem

In the last years, several drugs were approved for the treatment of HCV, including first and second generation protease inhibitors and RNA-dependent RNA polymerase inhibitors. Early first generation inhibitors were problematic due to adverse side effects as well as resistance development. Upon the establishment of second generation protease and polymerase inhibitors resistance development is strongly suppressed, but their potency seems limited against certain geneotypes.

Current HCV inhibitors usually target viral protease and RNA-polymerase, but targeting the HCV core protein, which forms the viral capsid, might be a very promising approach for the development of novel antiviral drugs. As the core protein is highly conserved, a drug targeting this protein could be expected to be active against all HCV genotypes. Moreover, other members of the family of Flaviviridae have very similar capsid proteins with conserved elements, which could provide a broad antiviral activity against a wide range of viruses.

Solution

The present invention relates to low-molecular weight compounds for the use in the prevention or treatment of a viral infection caused by an RNA virus, in particular to HCV, DENV but also to Zika virus, West-Nile virus, Yellow Fever Virus and others. *In vitro* cell culture experiments showed low half maximal inhibitory concentration (down to 0.05 µM) and a high half maximal cytotoxic concentration, especially for Dengue virus. Target validation experiments showed that the small compounds interact with the caspid proteins and thereby crosslinking them which blockst he release of infectious particles. *In vivo* testing in mice showed no toxicity at high concentrations, exterted microsomal and plasma stability. Altogether, the herein discovered compounds have superior antiviral activity against RNA viruses, in particular members of the family Flaviviridae, and less cytotoxicity, thus unwandted side effects can be minimized.