

Steroid-based compounds against Malaria

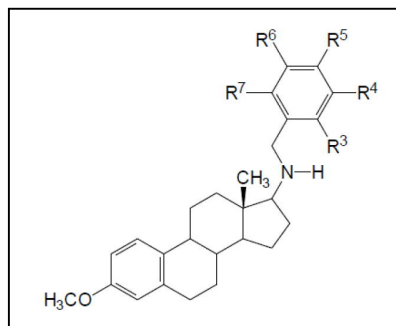
Highly effective / synergistic to artemisinin / no resistance / no side effects / upscaling possible

DESCRIPTION OF TECHNOLOGY / PRODUCT

A series of novel low molecular weight compounds with high activity against *Plasmodium falciparum* have been developed, synthesized and tested. The compounds are based on a substituted steroidal pharmacophore and are as anti-infective agents in their structure completely new.



Bild: Fotolia / Abele



The compounds are highly active against red blood cell stages of *P. falciparum*, also of chloroquine-resistant parasites. Present SAR data indicate that the hydrophobic steroid component and a hydroxyarylmethylamino group are essential for the antimalarial action of the compounds. The hydrophobic steroid part is likely to mediate membrane permeability.

SCOPE OF APPLICATION

The novel compounds are eligible for the development of new medicaments for the prophylaxis and treatment of Malaria or infections with the parasite *Plasmodium falciparum*, respectively.

The compounds are also suitable for the development of other antiparasitic therapeutics (e.g. against Schistosomiasis).

Furthermore, the compounds exhibit weak activity against fungi and moderate activity against selected bacteria (e.g. *E. coli*, *Mycobacterium vaccae*) and could therefore also be interesting for the development of antimicrobials.

AT A GLANCE ...

TECHNOLOGY FIELD / SCOPE OF APPLICATION

Therapy of Malaria and other infective diseases

MARKET / BRANCH

Pharma companies developing medicaments for the treatment of Malaria and other infections

USP

- Low nanomolar IC50 values in vitro (<2 ng/ml)
- More active than chloroquine or artesunate
- No known resistances
- No steroid-like side effects; very low cytotoxicity, no acute toxicity
- Upscaling possible
- Orally active
- Strongly synergistic to artemisinin

DEVELOPMENT STATUS

- ✓ Development of novel compounds based on steroidal pharmacophore
- ✓ Synthesis of ca. 60 derivatives plus series of non-steroidal analogs for SAR studies and lead optimisation
- ✓ Compounds tested in vitro
- ✓ Compounds tested in mouse model in vivo
- Next steps: systematic SAR studies, optimization of lead compounds, more detailed toxicology and ADME studies

PATENT PORTFOLIO

Patent granted in US, EP and India

REFERENCE NO.: **TM 518**

ADVANTAGES COMPARED TO STATE OF THE ART

Beside the high activity against *P. falciparum*, the inhibitors have a strong synergistic action with artemisinin and artesunate and exhibit a very low cytotoxicity and no acute toxicity in the mouse model.

Parasitemia in the mouse model could be reduced by 99.8% with the favorite compound in a dose-dependent manner i.p., all mice were cured.

The compounds are also orally active and reduced parasitemia by 99.78%. Two thirds of the animals were cured. Also a single dose reduced parasitemia by 98.46% and increased life span from 4 to 14 days.

The compounds are fast acting. The favorite compound was more active than chloroquine or artesunate

DEVELOPMENT STATUS

The compounds were synthesized and their activity against *Plasmodium falciparum* blood stages was demonstrated according to internationally accepted protocols.

In various cell culture experiments no major cytotoxic effects have been observed. The compounds were furthermore tested in vivo in a Malaria mouse model. The novel active substances were well tolerated by the mice, substantially reduced the parasitic load and exhibited a life-prolonging effect.

MARKET POTENTIAL

To date, approximately three billion people in 108 countries are threatened by infections with the Malaria pathogen *Plasmodium falciparum*. Annually, about 240 million people are diagnosed with Malaria of which an estimated number of one million die from this disease, and 90% of the people affected by Malaria come from Africa.

The number of infections also increases in other countries on other continents. According to estimations by the WHO, about 15 millions of people are annually infected by Malaria in India alone, of which about 20.000 die from this infection. This number corresponds to approximately 77% of the Malaria cases in the entire Southeast Asian region.

In 2008, the market for pharmaceuticals for the treatment of Malaria reached 118 million US-dollars alone in the countries of Nigeria, Kenya and Tanzania (Frost & Sullivan, 2008).

OFFER

On behalf of its shareholder Justus-Liebig-Universität Giessen TransMIT GmbH is looking for cooperation partners or licensees for further preclinical and clinical development of the compounds in Germany, Europe, the USA, and Asia.

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