Corallopyronin A as an effective anthelmintic

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Filariasis in humans and dirofilariasis in pets

• caused by nematodes, transmitted via blood sucking insects

• human filariasis
  a) lymphatic filariasis (elephantiasis):
    • 120 million infected
    • ~40% have disease
  b) onchocerciasis (river blindness):
    • 40 million infected
    • ~50% have disease

• dirofilariasis (heartworm disease):
  • infect more than 30 species of animals
  • large companion animal market
  • endemic in all States of the USA, especially in the South
Corallopyronin A targets the bacteria *Wolbachia*

- all worms harbor the bacterial endosymbiont *Wolbachia*
  - essential for worm development, fecundity and survival

- Corallopyronin A (Cor A) has efficacy against *Wolbachia*
  - *in vivo* results: depletion of >98% of *Wolbachia* → blocked larval development
Existing solutions – promising alternative CorA

Current treatment in humans:

a) target: the nematode
   - e.g. diethylcarbamazine, ivermectin
   - populations in endemic regions
     - treatment for many years
   - suboptimal responders are observed
     - possible resistance

b) target: Wolbachia
   - doxycycline, rifampicin
   - contraindication for children
   - rifampicin is given against tuberculosis
     - not used for filariasis to avoid risk of developing resistance in *M. tuberculosis*

beneficial alternative: Corallopyronin A
Corallopyronin A – a novel RNAP inhibitor

- MoA: binds “switch region”
  - active against rifampicin-resistant *S. aureus*
  - no cross-resistance, e.g. rifampicin

- good efficacy against Gram+
  - *E. coli tolC* mutants are sensitive
  - ineffective against *Mycobacterium* spp.

- is orally available in mice
  - equivalent to intraperitoneal injection

- is not cytotoxic
  - effective dose is 1 µg/mL
    - cytotoxicity seen at 20-200 µg/mL
  - no up-regulation of CYP450 expression
  - first evidence, that CorA will not induce negative drug-drug interactions
Corallopyronin A – a potential therapeutic agent

• PCT patent application is pending
  • positive search report

• next steps:
  • minimum dosage finding in susceptible rodents
  • primary pharmacodynamics and pharmacokinetics
  • in vitro CYP profiling
  • ADMET in rodents and dogs
  • development of a Galenic formula
  • further development of the production of CorA
    • optimization of purification, specification, stability tests)

• access to rights for commercial use of this invention and the opportunity for further co-development
Thank you for your attention!

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