COMPOUNDS FOR TREATING *HELICOBACTER PYLORI* AND *CAMPYLOBACTER JEJUNI* INFECTION

The present invention describes new bioactive compounds with antimicrobial activity against *Helicobacter pylori* (*H. pylori*) and *Campylobacter jejuni* (*C. jejuni*) by acting specifically on the protein HsrA (essential for cell viability).

Description

Helicobacter pylori and *Campylobacter jejuni* are considered "high priority" pathogens in the R&D of new antimicrobials by the World Health Organization due to their high risk for human heath because of increasing antibiotic resistance worldwide. *H. pylori* infection affects more than 50% of world population. Persistent colonization of human stomach by this pathogen results in gastric inflammation and highly contributes to the pathogenesis of peptic ulceration, gastric adenocarcinoma, and mucosa-associated lymphoid-tissue (MALT) lymphoma. Nearly 60% of the intestinal type gastric cancers and 98% of MALT lymphomas are associated with *H. pylori* infections. In addition, the presence of *H. pylori* in the host increases the risk of developing other lymphomas, such as diffuse large B cell lymphoma and ocular adnexal lymphoma.

Current treatments against *H. pylori* infection relie on a combination of three or more antimicrobial drugs and an antisecretory agent. A standard triple therapy containing a proton-pump inhibitor (PPI, usually omeprazole) and two antibiotics, clarithromycin and either amoxicillin or metronidazole, has been traditionally considered the first-line regimen Because of the increasing failure of the traditional triple therapy, current guidelines recommend a quadruple therapy (PPI + amoxicillin + metronidazole + clarithromycin) as first-line strategy. Bismuth-containing therapies or 10 days sequential therapies have been also proposed to replace standard triple therapy. Alternatively, levofloxacin-based triple therapies can be used as rescue therapy for *H. pylori* infection after failure of first-line regimens. However, the alarming increase in resistance to antibiotics, including levofloxacin, begins to limit the applicability of all such eradication therapies.

For its part, *C. jejuni* constitutes the main cause of bacterial gastroenteritis in humans worldwide. Although the infection usually produces self-limited diarrhea, it can trigger meningitis, bacteremia and hemorrhagic colitis that could be lethal in young children, immunocompromised and old population. The growing resistance of *C. jejuni* to antibiotics is becoming a public health problem.

Besides, current antimicrobial therapies against *H. pylori* and *C. jejuni* infection have negative side effects on normal human microbiota, which is a frequent cause of dysbiosis, therapy interruptions and emergence of antibiotic resistance.

Innovative aspects

The compounds of the invention are as effective as traditional antibiotics against *H. pylori* and *C. jejuni* while not being harmful to normal human microbiota.

Furthermore, these compounds are not affected by the molecular mechanisms of resistances developed by *H. pylori* and *C. jejuni*.

Therefore, these antimicrobial compounds may be of special relevance in the eradication of infections caused by strains resistant to conventional antibiotics.

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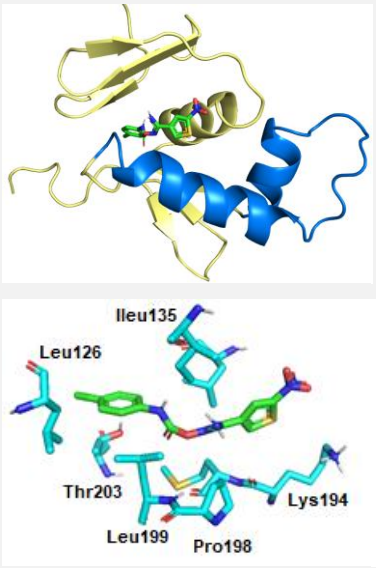

Model of the molecular interaction between the compounds of the invention and the C-terminal DNA binding domain of the *H. pylori* essential response regulator HsrA. The helix-turn-helix (HTH) DNA binding motif of HsrA has been highlighted in blue. Some interacting residues are indicated.

IPR status

Spanish patent application (2022) with extension possibilities.

Available for

Further research or development

Exclusive/non-exclusive licence agreement

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