TECHNOLOGY OFFER

ANTIMICROBIAL PYRAZINO [1,2-B]QUINAZOLINE-3,6-DIONES DERIVATIVES AND THEIR PRODUCTION

This invention relates to pyrazino [1,2-b] quinazoline-3,6-diones compounds, in particular it relates to pyrazino [1,2-b] quinazoline-3,6-diones compounds having antibacterial activity and/or antimalarial activity. The invention encompasses the synthesis and the use of synthetic pyrazino [1,2-b]quinazoline-3,6-diones derivatives, inspired by complex marine compounds with antimicrobial properties.

KEYWORDS

- Antibacterial agent
- Antimalarial agent
- Drug discovery
- *Plasmodium falciparum*
- Methicillin-resistant
- *Staphylococcus aureus*

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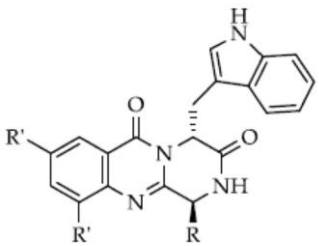
DESCRIPTION

Antibacterial resistance has increased dramatically, becoming an emergency in healthcare. Despite enormous efforts, the number of therapeutically useful compounds that aim for circumventing the resistance is continuously decreasing and no truly novel class of compounds has been introduced to a successful therapy.

In order to stop the clinical consequences of the development and spread of antimicrobial resistance both the preservation of current antimicrobials through their appropriate use, as well as the discovery and development of new agents are mandatory. Likewise, malaria represents a major threat to the public health worldwide. Along with widespread resistance to historical antimalarials, is emergent the need to identify new chemical diversity, ideally with novel antimalarial modes of action.



The invention encompasses the synthesis and the use of synthetic pyrazino [1,2-b]quinazoline-3,6-diones derivatives. Best lead compounds are potent antimicrobials against methicillin-resistant *Staphylococcus aureus* (MIC 4-8 µg/mL) and *Plasmodium falciparum* 3D7 (IC50 0.02-2 µg/mL). Molecular docking studies support the inhibition of gene expression of *Plasmodium* and *Leishmania* sp. via prolyl-tRNA synthetase.

ADVANTAGES & INNOVATIONS

One-step synthesis from cheap building blocks; Potent antimicrobial activity against multi-resistant bacterial pathogens and antimalarial activity; Compounds had no hemolytic nor cytotoxic effects at MIC/IC50 concentrations.

INTELLECTUAL PROPERTY RIGHTS

Patent status

International Patent Application via PCT WO2021033159

Priority date: 20.08.2019

Pending in EU, US

STAGE OF DEVELOPMENT

TRL 3 – Experimental proof of concept

COOPERATION OPPORTUNITY

Licensing agreement.

R&D partnership.

RELEVANT PUBLICATIONS

Long S, Duarte D, Carvalho C, Oliveira R, Santarém N, Palmeira A, Resende DISP, Silva AMS, Moreira R, Kijjoa A, Cordeiro da Silva A, Nogueira F, Sousa E, Pinto MMM. Indole-Containing Pyrazino[2,1-_b_]quinazoline-3,6-diones Active against Plasmodium and Trypanosomatids. ACS Med Chem Lett. 2022 Jan 11;13(2):225-235. https://doi.org/10.1021/acsmedchemlett.1c00589

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