Antibacterial Compounds

UNIVERSITÀ DI SIENA 1240

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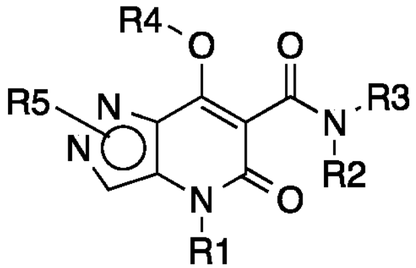
Invention

Defined as one of the most urgent medical needs in 2014, antibiotic resistance in Gram-positive and Gram-negative bacteria leads to increased morbidity and mortality rates in affected patients, heavily impacting on the public health system.

In order to counteract the emergence of multi-resistance, up to pan-resistance to (almost) all available classes of antibiotics, the compounds of the present invention are pyrazole[4,3-b]pyridin-6-carboxamide derivatives characterised by direct antibacterial activity against several Gram-positive bacteria (*Bacillus subtilis*, *Enterococcus faecalis*, *Streptococcus pyogenes*, *Staphylococcus aureus*). Furthermore, the compounds act synergistically with a second antibiotic of the polymyxin family (polymyxin E1) against resistant Gram-negative bacteria such as *Acinetobacter baumannii*, while restoring the sensitivity of the strains to the same polymyxins. The derivatives are both active against resistant strains and display no cytotoxic effects on host cells (as evidenced by *in vitro* tests). They are also potentially active against protozoa, fungi and viruses.

Medicinal preparations of the compounds of the invention, their salts, derivatives and pharmacologically acceptable excipients, in the presence or absence of additional antibiotics, may thus be used as treatments of multidrug-resistant bacterial infections.

Drawings & pictures



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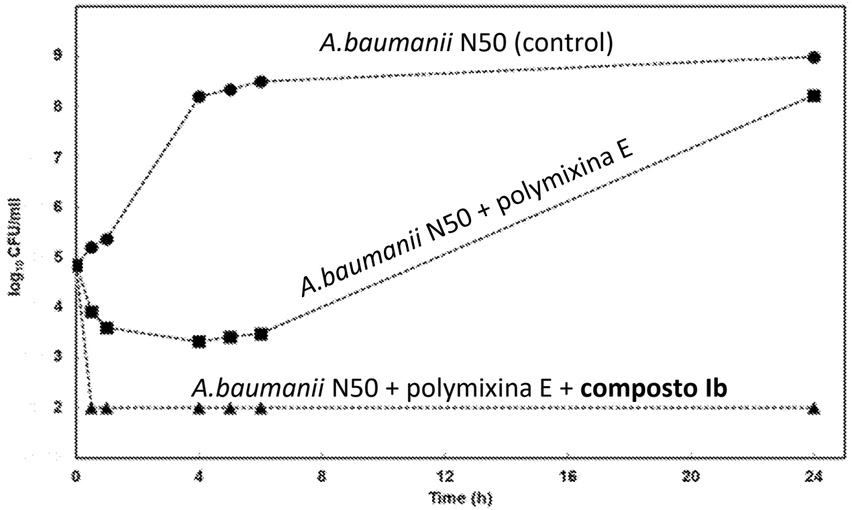
Compound	Bacterial strain	Average FIC index
Ib	*E. coli* CCUG^T	0.26
	K. pneumoniae ATCC 13833	0.30
	A. baumannii ATCC 17978	0.29
	A. baumannii N50[a]	0.30
Im	*K. pneumoniae* SI-4B[a]	0.31
	K. pneumoniae SI-27[a]	0.41
In	*K. pneumoniae* ATCC 13833	0.32
Ip	*K. pneumoniae* ATCC 13833	0.32
	E. coli CCUG^T	0.33
Ix	*K. pneumoniae* ATCC 13833	0.33
	A. baumannii ATCC 17978	0.27
	K. pneumoniae SI-4B[a]	0.39

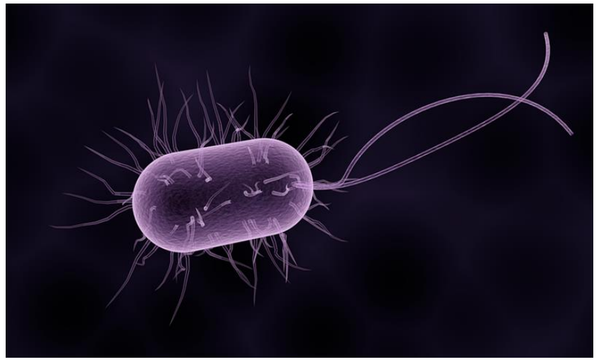
[a]strains resistant to colistin (MIC polymyxin E1≥ 4 mg/L)

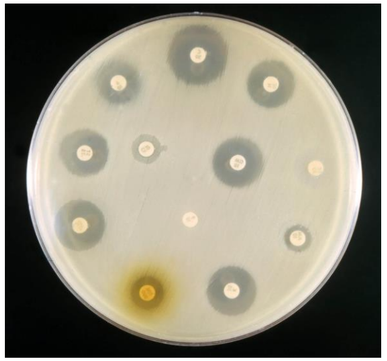


Industrial applications

The technology may be of interest in chemical and/or pharmaceutical companies having (or wishing to expand) in their pipeline drugs for the treatment of infectious agents.

In particular, the invention can be formulated to be compatible with different administration routes, such as topical, enteral, oral, parenteral, intranasal, intravenous or intrarterial, intramuscular, intravesical or intraurethral, subcutaneous, intraocular or the like, possibly with gradual and/or controlled release.





Possible developments

Currently evaluated at a TRL of 3, the technology can be further developed within specific technology maturation projects aimed at raising the level and thereby allowing introduction into the industrial network.

The group is looking for industrial partners operating in the pharmaceutical sector interested in collaborating on the aforementioned technological maturation of the invention.

The University of Siena is open to specific agreements aimed at the exploitation, licensing or option of the patented invention.

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