NEW ANTIBIOTICS TO FIGHT RESISTANT BACTERIA

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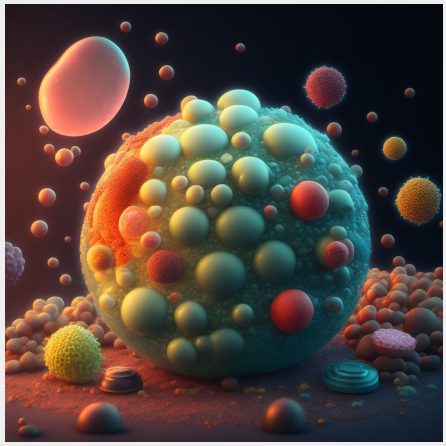
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ABSTRACT

The Institute of Organic Synthesis at the University of Alicante has discovered a new family of molecules that can effectively combat bacteria resistant to conventional antibiotics, including tuberculosis.

The innovation lies in the novel molecular structure of these compounds, and among their main advantages are their high antibiotic activity, their reduced degradation in the biological environment and the simple synthesis procedure.

Chemical and/or pharmaceutical companies interested in acquiring this technology for commercial exploitation through patent licensing agreements are sought.



INTRODUCTION

Antibiotic resistance is one of the greatest threats to public health worldwide. According to the World Health Organization (WHO), around 700.000 people die each year due to antibiotic-resistant infections, and it is estimated that this figure will rise to 10 million by 2050 if urgent action is not taken.

In addition, the development of new antibiotics has stagnated in recent decades, leading to a decrease in the availability of therapeutic alternatives.

Consequently, the need for new antibiotics is in great demand by society and, in fact, is one of the WHO's preferred lines of action.

Currently, the molecular structure 2-(pyrrolidin-1-yl)thiazole, and its respective carboxylic acid, has provided low antibacterial activity results. Therefore, there is a need to look for appropriate substituents in this type of molecular structure that would significantly increase the antibiotic power against resistant bacteria.

TECHNICAL DESCRIPTION

In order to solve the problems described above, **a new family of molecules has been discovered that can effectively combat bacteria resistant to conventional antibiotics**, including **tuberculosis**.

The present invention refers to a set of molecules or compounds with the following general formula (*see Figure 1*), as well as to a pharmaceutically acceptable formulation (ester, carboxylic acid or carboxylic acid salt) comprising at least one compound of the following formula:

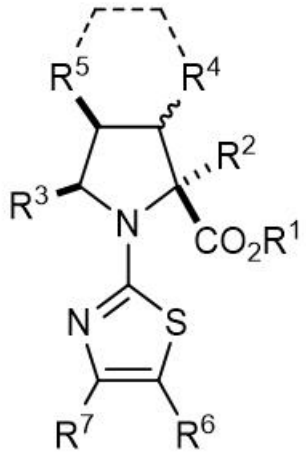


Figure 1: Thiazoles with a pyrrolidine ring as a substituent and their acid derivatives

These compounds can be synthesised in the laboratory in **three simple steps** under **mild reaction conditions**:

1. Pyrrolidine or pyrrolidine derivative is obtained by reaction of iminoesters and electrophilic alkenes via a 1,3-dipolar reaction (*see Figure 2*).

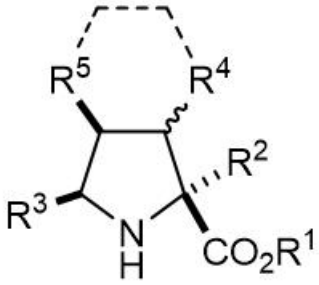


Figure 2.

2. A condensation reaction of the above pyrrolidines with benzoyl isothiocyanate is then carried out (*see Figure 3*).

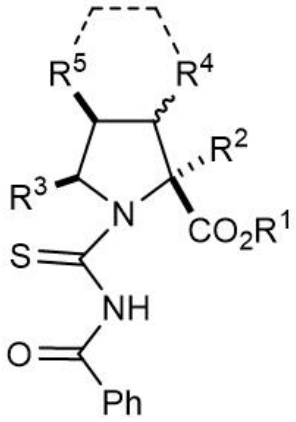


Figure 3.

3. Finally, haloketones are added to the synthesised thioureas to obtain the final thiazole-pyrrolidine structure (*see Figure 1*).

ADVANTAGES AND INNOVATIVE ASPECTS

ADVANTAGES OF THE TECHNOLOGY

This novel technology has the following advantages:

1) **Antibiotic efficacy** demonstrated in in vitro tests.

2) **Less degradation** in the biological environment.

3) **Greater therapeutic effect**.

4) **High antibiotic activity** against different bacteria resistant to conventional antibiotics.

5) **Greater specificity** towards antibiotic-resistant bacteria, including *Mycobacterium tuberculosis*, an infectious disease that is increasingly difficult to treat with existing antibiotics.

6) Enables treatment of infections that were previously difficult or impossible to cure due to bacterial resistance.

7) Potential to **prevent future resistance** by being effective against bacteria that have already developed resistance to other antibiotics.

8) **Wide field of application** in the field of pharmaceutical chemistry and medicine in general.

9) The synthesis procedure of these compounds is **very simple**: only three steps.

10) The synthesis procedure is carried out under **mild reaction conditions**.

11) The synthesis procedure allows **good yields** of the final compound.

Its potential to save lives and prevent future resistance makes it a valuable and promising technology for the future of medicine.

INNOVATIVE ASPECTS OF THE TECHNOLOGY

The main innovation lies in the **molecular structure** of these chemical compounds, which allows them to be effective against bacteria that have developed resistance to other antibiotics, representing a very significant advance in the effective fight against this type of bacteria, which is a growing and worrying problem worldwide.

The new compounds described in this patent can treat a **wide variety of infections** caused by resistant bacteria, which can significantly improve the therapeutic options available.

These molecules can be used as active species against different types of microorganisms, preferably in the prevention and/or treatment of infections such as tuberculosis.

CURRENT STATE OF DEVELOPMENT

The technology described is at an early stage of development (Technology Readiness Level: **TRL = 4**), but has great potential to address one of today's greatest medical challenges: antibiotic resistance.

These compounds have been shown to be **effective in *in vitro* assays at the laboratory level**, suggesting that they have great potential to be a valuable tool in combating infections caused by resistant bacteria. However, more clinical trials are still needed to determine the safety and efficacy of these new compounds in humans.

The patent describes several specific examples of chemical compounds and their antimicrobial activity against different bacterial strains.

The cytotoxic activity of the molecules described in the present invention was tested using different lines of microorganisms to establish their antimicrobial efficacy in *in vitro* studies. For this purpose, antibacterial assays were performed with different molecules against standard bacterial strains of *Staphylococcus aureus* [ATCC 25925], *Bacillus subtilis* [ATCC 6633], *Aeromonas hydrophila* [ATCC 95080], *Escherichia coli* [ATCC 25923] and *Acinetobacter baumannii* [ATCC 02026]).

An anti-tuberculosis assay was also performed to determine the minimum inhibitory concentration (MIC) of the newly synthesised compounds against the standard strain H37Rv of *Mycobacterium tuberculosis*.

The bioactivity results correlate with the presence of different substituents at various positions of the general formula structure (*see Figure 1*), and may **induce higher bioactivity** by modifying certain substituents at specific positions.

MARKET APPLICATIONS

This new set of molecules can be applied in:

- **Pharmaceutical industry**: the new compounds described in the patent have the potential to be used as antibiotics to treat a wide variety of infections caused by resistant bacteria.
- **Medical sector**: the new compounds can be used to treat resistant bacterial infections in patients.
- **Scientific research**: the technology can be used to research and develop new antimicrobial compounds.
- **Agricultural sector**: the new compounds can be used as antimicrobial agents in the production of food and animal feed.
- **Veterinary sector**: the new compounds can be used to treat resistant bacterial infections in animals.

One of the main benefits of this technology is its ability to treat infections caused by bacteria resistant to conventional

antibiotics. For example, tuberculosis is an infectious disease caused by the bacterium *Mycobacterium tuberculosis*, and has become increasingly difficult to treat due to resistance to existing antibiotics. In this sense, the new compounds described in this patent have the potential to be **effective against resistant strains of *Mycobacterium tuberculosis***.

COLLABORATION SOUGHT

Currently, there are no commercial products related to these structures. In this sense, companies interested in acquiring this technology for **commercial exploitation** through **patent licensing agreements** are sought.

Company profile sought:

- Pharmaceutical industry.
- Chemical industry.

INTELLECTUAL PROPERTY RIGHTS

The present invention is protected through **patent application**:

- *Patent title: "Compuestos 2-(Pirrolidin-1-il)tiazoles, su proceso de fabricación y su uso como agentes antibióticos".*
- *Application number: P202230725.*
- *Application date: 4th August 2022.*

MARKET APPLICATION (2)

Medicine and Health
Chemical Technology

TECHNICAL IMAGES (1)

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