Targeting bacterial cell division to fight antibiotic resistance

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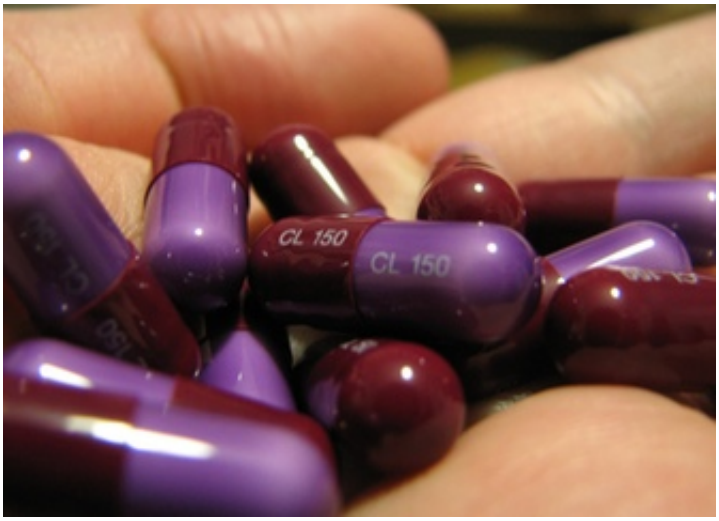

Credit: lamentables

New research has found some compounds effective in blocking the proliferation of certain bacteria, raising hopes of a new class of drugs to combat antibiotic resistant infections.

Nowadays, people do not expect to die as a result of a common infection like bacterial pneumonia. However, many do. Indeed, some bacteria have become resistant to all available antibiotics, due to overuse. The trouble is that there are currently no antibiotic that can kill all possible pathogens. Until now, antibiotic resistance has been counteracted by isolating derivatives of the antibiotics that are less easily degraded or

expelled by the bacteria, by working on chemical modifications of the available antibiotics or by giving a combination of the antibiotics available. But scientists insist on the need to come up with a new class of antibiotics to avoid the dawn of a post-antibiotic era where such drugs no longer work.

Now, DIVINOCELL, an EU funded research project, has opened the way for a new strategy to develop antibiotics. Specifically, its approach is based on creating antimicrobial compounds designed to interfere with proteins involved in cell division, which will block the pathogen's proliferation. "We have studied how Gram-negative bacteria proliferate to find those proteins that are specifically sensitive to inhibition," explains Miguel Vicente, an expert in bacterial cell division at the National Centre of Biotechnology, in Madrid, Spain. So-called Gram-negative bacteria are a type of bacteria, which tends to be more resistant to antibiotic because of the complex structure of their outer layer, which does not easily allow antibiotics entry.

The strategy is untested, at yet. "We expect that if we find a compound that can inhibit the activity of any of these proteins, the bacteria will not proliferate," Vicente, who is also the project coordinator, tells youris.com, "and consequently we will have initiated the discovery of a new antibiotic."

Already, there has been some progress. Currently, "the compounds we have discovered are not active at the low concentrations needed for their clinical use," Vicente points out, adding that their toxicity and their ability to be excreted from the body is yet unknown. All in all, it may take 12 to 15 years for such compound to go from the laboratory to the pharmacy.

Experts agree. "One main challenge of the project will be testing and reducing the toxicity of these compounds, as they will have to get

companies interested in investing in large and costly clinical trials," comments Diarmaid Hughes, professor of medical molecular bacteriology at Uppsala University, in Sweden.

The lengthy drug development process could also be hampered by the need to have a viable business model. "Now, additional research is needed to transform the most promising compounds into what the industry calls a [drug] lead and then into a [drug] candidate," Vicente notes, "but this is a very lengthy and costly process and antibiotic consumer pattern—that are to be taken only once, not like chronic treatments—does not yield sufficient benefits to incentivise research to develop a new antibiotic."

To counteract this lack of appeal for pharmaceutical companies the EU has funded the ENABLE project, launched in February 2014, to support the development of new antibiotics against Gram-negative bacteria. It is part of the Innovative Medicines Initiative aimed at finding economic models that make research on new drugs more interesting for companies. "The important thing is that all these funded programs show that Europe and the US are taking the problem seriously," Hughes tells youris.com. "We observe a correlation between the total amount of use of antibiotics and resistance problems", adds Hughes. According to ECDC's 2013 Annual Epidemiological Report, in 2011, the percentage of E.coliisolates resistant to third-generation antibiotic called cephalosporins ranged from 3% in Sweden to 36% in Cyprus and showed a clear north-to-south gradient.

Other experts believe that there is a need to better manage the adminstration of new classes of antibiotics to avoid resistance. "It is really important that researchers look for new antibiotics but, at the same time, it would be such a waste of time and money if these antibiotics would come to the market and just be handled in the same irrational way, as we have been doing with the previous generations," says Erika

Vlieghe, a clinical infectiologist at the Institute of Tropical Medicine, in Antwerpen, Belgium. She is a specialist in low income countries where the impact of antibiotic resistant infections is even higher. She concludes: "We need a structure that ensures that these new antibiotics will be used under both the right prescription and the right indication."

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