

## Now we know why old scizophrenia medicine works on antibiotics-resistant bacteria

## May 17 2013

In 2008 researchers from the University of Southern Denmark showed that the drug thioridazine, which has previously been used to treat schizophrenia, is also a powerful weapon against antibiotic-resistant bacteria such as *staphylococci* (*Staphylococcus aureus*).

Antibiotic-resistant bacteria is a huge problem all over the world: For example, 25 - 50 per cent of the inhabitants in southern Europe are resistant to *staphylococci*. In the Scandinavian countries it is less than 5 per cent, but also here the risk of resistance is on the rise.

So any effective anti-inflammatory candidate is important to investigate - even if the candidate is an antipsychotic that was originally developed to alleviate one of the hardest <u>mental illnesses</u>, schizophrenia.

Until now, scientists could only see that thioridazine works effectively and that it can kill *staphylococcus* bacteria in a flask in the laboratory, but now a new study reveals why and how thioridazine works. The research group, which includes professor Hans Jørn Kolmos, associate professor Birgitte H. Kallipolitis and other participants from the Department of Biochemistry and Molecular Biology and Institute of Clinical Medicine, University of Southern Denmark, publishes their findings in the journal *PLOS ONE* on May 17 2013.

The research team tested thioridazine on *staphylococcal* bacteria and discovered that thioridazine works by weakening the <u>bacterial cell wall</u>.



"When we treat the bacteria with antibiotics alone, nothing happens - the bacteria are not even affected. But when we add both thioridazine and antibiotics, something happens: thioridazine weakens the bacterial cell wall by removing glycine (an amino acid) from the cell wall. In the absence of glycine, the antibiotics can attack the weakened cell wall and kill *staphylococcus* bacteria", explains Janne Kudsk Klitgaard, visiting scholar at the Department of Biochemistry and Molecular Biology, University of Southern Denmark.

Thus, it is the interaction between thioridazine and antibiotic that works.

And now that researchers know that thioridazine works by weakening *staphylococcal* cell wall, they can concentrate on improving this ability.

"Now that we know how thioridazine works, we can develop drugs that target the resistant <u>bacteria</u>. And just as important: We can remove or inactivate the parts of thioridazine, which treats schizophrenia, so we end up with a brand new product that is no longer an antipsychotic, "explains Janne Kudsk Klitgaard.

According to her, we are now a little closer to a safe, nonpsychopharmacological drug that can save people from potentially fatal infections that do not respond to antibiotics.

"This will no longer be an <u>antipsychotic</u>, when scientists are finished with this task," she says.

Together with her colleagues Klitgaard tested thioridazine on roundworms in the laboratory and have seen that they were cured of *staphylococci* in the gut. Next step will be testing on mice and pigs.

Provided by University of Southern Denmark



Citation: Now we know why old scizophrenia medicine works on antibiotics-resistant bacteria (2013, May 17) retrieved 30 April 2024 from <a href="https://medicalxpress.com/news/2013-05-scizophrenia-medicine-antibiotics-resistant-bacteria.html">https://medicalxpress.com/news/2024 from</a> <a href="https://medicalxpress.com/news/2013-05-scizophrenia-medicine-antibiotics-resistant-bacteria.html">https://medicalxpress.com/news/2013-05-scizophrenia-medicine-antibiotics-resistant-bacteria.html</a>

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