Antibiotics found to have unexpected effects on mitochondria

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Antibiotics strongly affect the growth of this plant, A. thaliana.

An EPFL study has shown that tetracycline-based antibiotics have an unexpected effect on the development of many organisms. In addition to pointing out the issue of soil pollution by these antibiotics, which are widely administrated to livestock, the scientists call upon colleagues to explore the consequences of using them in experiments that modulate gene expression.

No one assumes that antibiotics are completely harmless. But a new study shows that some of them have unexpected consequences on the development of a wide variety of organisms. Scientists have observed significant effects in concentrations similar to those found in the soils in which our food crops are grown.

Since the discovery of penicillin in the first half of the 20th century, antibiotics have been a boon to medicine for their effectiveness in combating bacterial infection. Over the past few decades, the use of new generations of drugs based on specific molecules known as tetracyclines has become very widespread. They act on bacterial gene expression, weakening, stimulating, or shutting it down altogether.

This ability to act directly at the level of gene expression has also led many scientists to use tetracycline antibiotics in research.

Suffocating mitochondria

But a study done at Ecole polytechnique fédérale de Lausanne (EPFL, Switzerland), published today in the scientific journal *Cell Reports*, calls for caution when using this family of antibiotics. The scientists, led by Norman Moullan and Laurent Mouchiroud from EPFL's Laboratory of Integrative and Systemic Physiology (Nestlé Chair in Energy Metabolism), directed by Professor Johan Auwerx, observed that these molecules have a significant effect on mitochondria, the cell's "powerhouses."

"It's not that surprising, given that mitochondria are historically bacteria that evolved within our cells," says Mouchiroud. "A lot of attention has been paid to the role of antibiotics on our intestinal flora, which has ten times more cells than the rest of our bodies. However, the effects of antibiotics on our mitochondria, which themselves far outnumber the bacteria in our gut, haven't yet been studied in detail."

In collaboration with two other research teams, one Swiss (Bart DePlancke) and one Dutch (Riekelt Houtkooper), the EPFL scientists revisited data from previous studies from this angle and carried out new experiments using animal and plant cells.

Delayed development

The effects were huge. "After several days of treatment with high doses of doxycycline, mitochondrial respiration was visibly altered," explains Moullan. More surprising still, the consequences were observed all the way down the food chain, from mammals to flies to nematode worms to plants. "The worms' development was hindered. On the other hand, signs of aging appeared more slowly, something we had observed in earlier studies ."

The scientists also carried out growth tests on Arabidopsis thaliana, a common plant that's frequently used in laboratory research. After growing for a week on a normal substrate, it was transplanted into soil with varying concentrations of doxycycline. "Delays in growth, some quite severe, were observed after a few days, even in soils in which the concentration of antibiotics was no stronger than is found in some agricultural soils today," says Moullan.

From forage to field

This pollution whose consequences are just beginning to be appreciated is caused by the widespread administration of antibiotics to livestock. "Because they are give orally in feed, they are only partially digested and end up in manure, which is then spread on the fields," explains Mouchiroud.

The quantities involved are huge, and the economic stakes equally sobering. In 2011, 5.6 million kg of tetracycline was administered to US livestock. A study showed that nearly half of the 210 kg of antibiotics produced in China in 2007 were tetracyclines for veterinary use. "The effects on growth of plants other than A. thaliana have not yet been studied, but our work indicates a need for caution," says Moullan.

The researchers also call on their scientific colleagues to be more careful when using antibiotics in experiments for modulating gene expression. "You observe the effect you're looking for, but you lose sight of the fact that these substances have serious consequences for overall metabolic function," says Mouchiroud.

Provided by Ecole Polytechnique Federale de Lausanne