Marine compound first new natural antibiotic in decades

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It's a big world out there. Credit: Ronaldhole

A new antibiotic that is effective at killing anthrax and superbug MRSA bacteria could be a weapon in the fight against antibiotic resistance – and terrorism.

Anthracimycin, a chemical compound derived from the Steptomyces bacteria, was discovered in the ocean off the coast of Santa Barbara in California. Its unique chemical structure makes it a new addition to the antibiotic family that could pave the way for new drugs.

Most new antibiotics are derivatives of existing compounds. The last new naturally-derived antibiotic that entered the market was Daptomycin, a soil-derived compound from Streptomyces roseosporus, approved a decade ago in 2003. It was originally discovered in 1986.

"The discovery of truly new antibiotic compounds is quite rare," said William Fenical, Professor of Oceanography and Pharmaceutical Science at the Scripps Institution of Oceanography at UC San Diego, who led the research team.

"It's not just one discovery," he said. "It opens up the opportunity to develop analogues – potentially hundreds. Alexander Fleming discovered Penicillin in the 1928 and from that more than 25 drugs were developed. When you find a new antibiotic structure, it goes beyond just one."

MRSA and anthrax

Initial tests suggest that Anthracimycin is particularly potent against MRSA and anthrax, Bacillus anthracis, a lethal bacterial infection that is commonly associated today with outbreaks in livestock and its threat as a biological weapon – particularly after it was deliberately spread in the US mail following the 9/11 attacks in 2001.

The team tested the compound on lab mice infected with MRSA – which would have killed within five days. At at 1mg dose per 1Kg of a mouse's weight, it proved effective in eradicating the infection in about 85% of mice.

MRSA (meticillin-resistant staphylococcus aureus) can cause life-threatening infections and has been a scourge in hospitals because it is resistant to a number of widely used antibiotics.

Antibiotics are highly effective in treating anthrax but it would also

possible for terrorists to manufacture a drug resistant strain from known antibiotics, Fenical said. The new discovery could be used by a government to develop an antibiotic that was withheld from public consumption for emergency use.

The team has openly published their findings in the German applied chemistry journal *Angewandte Chemie* for pharmaceutical companies and governments that may be interested in starting research and development (RND) programmes.

Ocean discoveries

Drug companies carry out RND to discover new compounds and ultimately new drugs. This may be through engineering synthetic compounds or through the discovery of new ones in nature – building on the known healing properties in plants for example – or discovering entirely new compounds.

These can come from many sources including fungi and bacteria and environments such as the rainforest, or in the case of this new discovery, the ocean.

Between 1981 and 2006, around 63% of small molecule new chemical entities were derived from nature or from synthesising derivatives of natural products.

Penicillium was derived from the Penicillium fungus and was produced by the fungus as a defence mechanism against other microbes. Quinine, widely used in treating malaria, is an alkaloid extracted from the bark of the Cinchona tree in Latin America and Africa.

Some muscle relaxant drugs used alongside anaesthetics in surgery derive from the South American Curare plant. It's also used in drugs to

treat muscular diseases such as multiple sclerosis and Parkinson's disease. Streptomyces has produced a number of antibiotic, antifungal and antiparasitic drugs. However, new drug discovery and development is expensive and difficult.

"The potential for discoveries in oceans is enormous," said Fenical. "It's by far the largest biodiversity resource we have. It's a 3D resource too – it has animals, plants, microbes and when you reach the bottom there's an incredible richness of micro-organisms. But many regions are unexplored.

"But pharmaceutical companies don't have the expertise or the inclination to make ocean discoveries. There are about six marine-derived drugs in circulation and another 26 in clinical trials – including Marizomid and Plinabulin – but these discoveries have been made by academics. A lot of them are in the field of cancer and serious pain control and inflammation."

Drug resistance

The 1940s to 1960s were a golden era of antibiotic discovery, but since then research and discoveries have dropped significantly.

"No new natural antibiotic structures have been developed since 2003," said Fenical. "What's happening is stagnation. Anything that's approved tends to be a derivative of an existing structure. And sometimes within months there's a resistance to it."

Governments are often blind to the issue of resistance, he said, so there is a lack of funding for research from pharmaceutical companies.

Experts have been warning about a health crisis caused by antibiotic resistance and Sally Davis, the UK's chief medical officer, warned

earlier this year that the situation was so serious that it should be added to the government's national risk register of civil emergencies. She warned an "apocalyptic scenario" in 20 years' time could see people dying from routine infections after surgery because of a lack of antibiotics that work.

Antibiotics are used to treat serious infections but are also routinely used – and overused – to treat non-bacterial infections and in some countries sales to the general public is widespread. Their use in intensive farming has also caused concern.

But the lack of new discoveries and funding in research is an issue of global importance.

Laura Piddock, Professor of Microbiology at Birmingham University, said unless governments stimulated the development of new treatments, antibiotic resistance and the lack of new ones would soon become an unprecedented crisis.

"Across the globe, there needs to be action by all governments to increase funding for research into antibiotic resistance so that we can fully understand how it occurs, how it is spread … This information is essential if antibacterial discovery, research and development is to find and produce new treatments."

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