A marine mold substance that protects human cells against herbicide

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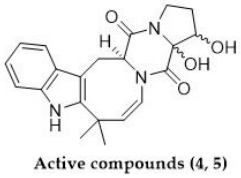

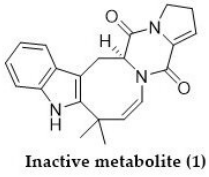

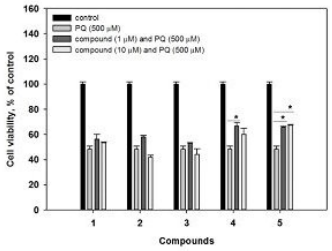

Penicillium dimorphosporum, the marine-derived fungus which has been cultivated in a lab. Credit: FEFU

Biologically active compounds from the marine fungus Penicillium dimorphosporum protect cells from paraquat, the highly toxic herbicide with no remedy, and might enhance the action of some drugs. The fungus was isolated from soft coral collected in the South China Sea during an expedition on the Akademik Oparin research vessel. Scientists

of Far Eastern Federal University (FEFU) and G. B. Elyakov Pacific Institute of Bioorganic Chemistry reported the results in *Marine Drugs*.

Paraquat is an herbicide compound highly toxic for animals and humans. About 100 countries, including the United States, apply it for crop cultivation and weed control. Dozens of countries, including Russia, have banned the poisonous compound. The problem of paraquat harm to people is widely known in India. Farmers who work in the fields risk dying from a dangerous dose of the substance.

FEFU specialists, together with Russian and foreign colleagues, have found that compounds from the marine-derived fungus Penicillium dimorphosporum might protect the cells against the effects of paraquat. The experiment was carried out on a neuroblastoma cell line. These are tumor cells adopted for studying the neuroprotective activity of forthcoming drugs.

"At a very low concentration, about one micromole per liter, the compounds fortified the viability of cells treated with paraquat by almost 40% compared to cells treated with paraquat alone. As a further step, we want to clarify the mode of action of these protecting natural molecules. Perhaps they act as antioxidants, and, probably, they can also secure cells from other toxic substances," said Olesya Zhuravleva, Head of the Laboratory of Biologically Active Compounds at the FEFU School of Natural Sciences.

According to the scientist, many active natural compounds have the disadvantage of low production in the host organism, so their quantity is not enough for in-depth study.

The case of Penicillium dimorphosporum is no exception. The fungus does not synthesize active compounds. However, scientists noticed an interesting feature of the fungus metabolism, which might overcome this

limitation. The fungus produces a broad range of isomeric compounds, as well as their biogenetic precursor. That means they have the same elements in the composition but differently structured. It looks like a kind of natural crooked mirror, where the set of atoms is reflected many times and in different ways. That provides the compounds with many functions that could be modified by scientists. Usually, the synthesis of a large number of isomers is not typical for living organisms.

"In this regard, we plan to scrutinize not the active natural compound itself, but its precursor, synthesized by the fungus abundantly, which we can modify up to the active state. That would be a successful step because the minor substance is much more difficult to get from a natural source than to adapt the major inactive precursor. For example, the fungus produces 200 milligrams of an inactive compound that we can customize and as little as 6 milligrams of an active natural substance. Many medicinal compounds are obtained in a similar semi-synthetic way, which allows avoiding complex and expensive complete synthesis," said Olesya Zhuravleva.

Next, the scientists plan to study in detail the neuroprotective mechanism of the selected active compounds, as well as prospects of using them in a combination with other existing compounds. According to the hypothesis, active molecules of the sea fungus might enhance the effect of some known drugs.

More information: Olesya I. Zhuravleva et al, New Deoxyisoaustamide Derivatives from the Coral-Derived Fungus Penicillium dimorphosporum KMM 4689, *Marine Drugs* (2021). DOI: 10.3390/md19010032

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