New ways to make plant-based medicines in space and on earth

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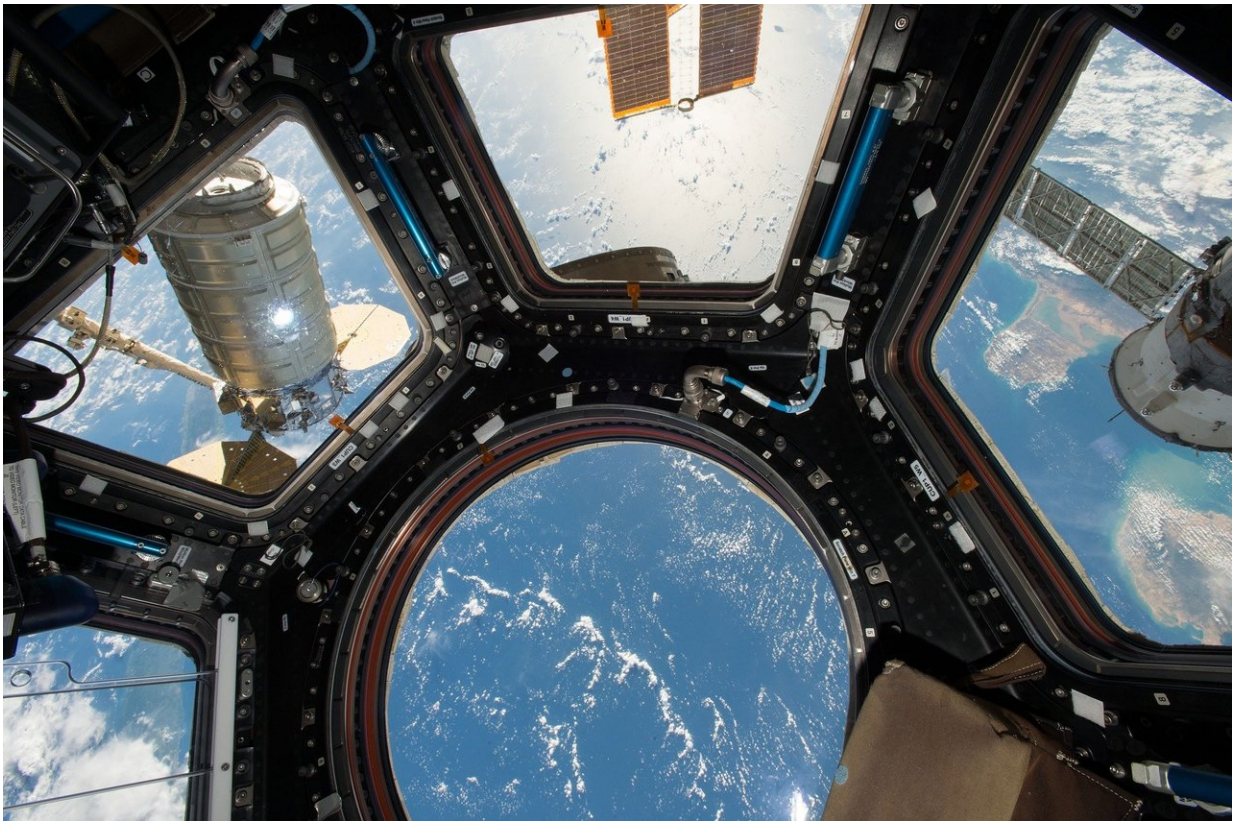

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How can you make medicines in space?

It's a difficult question, since many medicines we enjoy on Earth use

chemicals that come from plants, and space is nearly devoid of plants' basic needs: soil, water, oxygen and sunlight. At the same time, any realistic chance for future space exploration is going to require a way to treat illnesses without making a potentially months-long trip back to Earth.

John D'Auria, an assistant professor in the Texas Tech University Department of Chemistry & Biochemistry, has been instrumental in helping solve that problem in a way that also has more immediate ramifications here at home.

According to a study published today in the online journal *Nature Communications*, D'Auria and his colleagues report that, by discovering the genes and enzymes plants use to form the second ring in tropane alkaloids' core structure, they will be able to develop new, novel ways to produce these important chemicals.

"The bigger picture here is certainly the ability to start making these compounds in organisms that usually don't make them, i.e. bacteria, yeast and other plants," D'Auria said. "Compounds like this are great candidates for engineering in yeast or bacteria because we can then use them as substitutes for classical organic synthesis for the prospects of space exploration.

"There are no petrochemicals in space. That means if we want to make complex organic molecules, we will need to use bacteria, yeasts and plants to make them for us. This is the ultimate goal of our grant, and the paper is a major step on that road."

Of course, use in space isn't the only application of this research. Having new ways to produce tropane alkaloids also helps create medicinal compounds on Earth.

"Two tropane alkaloids, known as atropine and scopolamine, are listed by the World Health Organization as belonging to the essential list of modern pharmaceuticals," D'Auria said. "Atropine, for example, is what dilates your pupils when you go to the eye doctor. Scopolamine is commonly used as a motion sickness medicine and for patients who are nauseous from chemotherapy. Understanding how these compounds are made biochemically can help with their production in bacteria and yeast for a 'green chemistry' type of minimal impact, as well as aiding in designing new variants for medicinal use."

D'Auria's collaborators on the research include Cornelius Barry, Matt Bedewitz and Daniel Jones from Michigan State University as well as the laboratories of Texas Tech Horn Professor Guigen Li and associate professor Michael Findlater.

"I feel like we've made a great leap in understanding a class of plant-derived chemicals that are critical for human health," D'Auria said. "The potential this provides my research at Texas Tech cannot be understated. My students, both graduate and undergraduate, are embarking on a set of projects that will definitely wind up as major breakthroughs in metabolic engineering and synthetic biology.

"Of course, this work is also crucial to showing Texas Tech that our lab is gaining momentum and that, while our research may take longer than what is generally considered average for the fields of chemistry and biochemistry, the payoff is producing very impactful scientific journals."

More information: Matthew A. Bedewitz et al. Tropinone synthesis via an atypical polyketide synthase and P450-mediated cyclization, *Nature Communications* (2018). DOI: 10.1038/s41467-018-07671-3

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