Lee Silverberg, LVACS Member and PSU/Schuylkill chemistry professor, creates novel compounds shown to manage parasites

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By Samantha L. Bower, PSU News

SCHUYLKILL HAVEN, Pa. — Lee Silverberg, associate professor of chemistry at Penn State Schuylkill, has recently published a peer-reviewed paper on a novel method he has devised to create organic compounds that have demonstrated antiparasitic properties. Until this research was conducted, the structure of the starting material used to synthesize the chemical compounds was unknown.

Collaborating across the sciences

Collaboration is critical to Silverberg's research, and this project presented ample opportunity for it. For starters, creating these organic compounds allowed Silverberg to involve undergraduate students in his classroom.

"My students were involved in creating the compounds that we made and shared with biological scientist partners," said Silverberg. "The students are credited as collaborators in the new article published in 'Molecules.'"

This chemical research has biological implications, and collaborating across the sciences helped the chemical and biological scientists reach new informational heights. To expand upon the practical applications of these new compounds, Silverberg shared them with Megan Povelones, assistant professor of biology at Villanova University, who specializes in parasites.

Silverberg met Povelones when she worked at Penn State Brandywine, and the two have maintained contact since. "I met Megan at one of our University College Science Division meetings when she was still at Penn State," said Silverberg. "One of my end goals is that we make these compounds and get them to people who can test them for useful biological activity."

His collaboration with Povelones has been fruitful, and her work is a perfect complement to Silverberg's chemistry.

"We make all these compounds, and then we get these compounds to other people, like Dr. Povelones, to see what they can do with them," said Silverberg.

Silverberg's curiosity has also expanded the existing body of knowledge regarding the materials with which he has been working. The compounds Silverberg has been creating, known broadly as 1,3-thiaza-4-one heterocycles, are cyclic ones with sulfur and nitrogen in the ring. Through his literature review, Silverberg discovered that there was uncertainty as to what the structure of starting material thionicotinic acid looked like. With help from Hemant Yennawar, research professor of biochemistry and molecular biology and director of the X-Ray Crystallography Facility at Penn State University Park, he determined some crystal structures of this starting material.

"We nailed it down; we know the structure now," said Silverberg.

Practical applications in health care

The method Silverberg and his undergraduate students employ to synthesize these compounds is novel. “I’m inspired to make new compounds and make them in new ways,” said Silverberg, “and we’ve been doing just that.” Once the compounds are created, Silverberg sends them off to his peers.

Because she specializes in parasite biology, Povelones applied Silverberg’s compounds to Crithidia fasciculata, a parasite that does not in itself cause disease but is similar to others that do, and Trypanosoma brucei, another parasite that causes African sleeping sickness. This disease causes headaches, weakness, fatigue, and more, and can be fatal if left untreated.

To apply these compounds to the parasites, the biologists begin by dissolving the compounds in a solvent and then exposing parasites to the resulting solution. Povelones wanted to know what the best compound, a diphenyl pyridothiazinone, might do to the parasite, and discovered that it interrupted the parasite’s cell cycle and made them grow more slowly.

Silverberg synthesized 14 pyridothiazinone compounds for the “Molecules” paper, and five of the compounds have shown promise in managing the parasites. “Some of the compounds killed the parasites and killed them fast, but now we have to investigate how it works,” Silverberg said. “Our results are too preliminary to make any definitive determinations right now.”

Continuing the collaboration and further research opportunities

While Silverberg said he enjoys the fruits of his newly published paper, he sees ample opportunity for future research projects.

“One thing this project means to future research is that I have prioritized making these compounds. I am, at the moment, prioritizing it above everything else,” said Silverberg. “We had just so happened to finish creating a bunch of the compounds that showed the most activity here,” he added, commenting that he and his undergraduates will continue on this trajectory.

The next step in this research is determining how the compounds kill the parasites. Silverberg’s biological sciences collaborators will work on ranking the compounds in order of their efficacy against the parasites and identify which one is the most potent. From there, they will work to discover the mechanism by which the compound is killing parasites.

“Is the mechanism the same in that it inhibits cell growth, or is it something else?” Silverberg queried.

For the foreseeable future, Silverberg will keep trying to make these compounds and get them tested.

“I have 10 different projects going in various stages, and they're all related, but they're also all somewhat different in some way,” he commented.

Fascinating findings

As he completed this project, Silverberg was excited by some of what he believes to be the more mundane aspects of the chemistry.

“I thought it was interesting that these specific compounds were really easy to crystallize out. It makes purification easy,” he said.

And there are several reasons to be excited about this work. “I'm thrilled about what the compounds do to the parasites. We were able to make all of the compounds we tried to make, and they came out in pretty good yields. I'm happy and fascinated by this X-ray structure we got because it's unique. Even though it wasn't a goal of this research, it's just one of those things that has been enjoyable to see. But I'm a chemist, so the chemistry interests me,” he concluded.