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Introducing the Researcher ❷

Assistant Professor Yoko Saikawa investigates into and identifies materials responsible for natural phenomena.

Shedding Light on Various "Whys" in Our Daily Lives

Explaining toxicity of a mushroom by chemical approach

Yoko Saikawa

Why is hippopotamus sweat red? . . . There are so many "Whys" in our daily lives and in the world. Assistant Professor Yoko Saikawa of the Natural Product Chemistry Laboratory investigates into materials responsible for a variety of natural phenomena. She recently identified the toxic component of the poisonous *Russula subnigricans* mushroom.

The *Russula subnigricans*, popularly known in Japan as "Nise Kurohatsu" (see photo below), looks truly tasty but is actually a poisonous mushroom. It was first announced as a mushroom of fatal toxicity during the 1950s. But it has almost been forgotten because no accidental deaths were reported during the ensuing 50 years and also because there are several other similar-looking mushrooms.

In July 2009 the British scientific magazine *Nature Chemical Biology* carried an article announcing that the poison in *Russula subnigricans* mushroom is cycloprop-2-ene carboxylic acid.

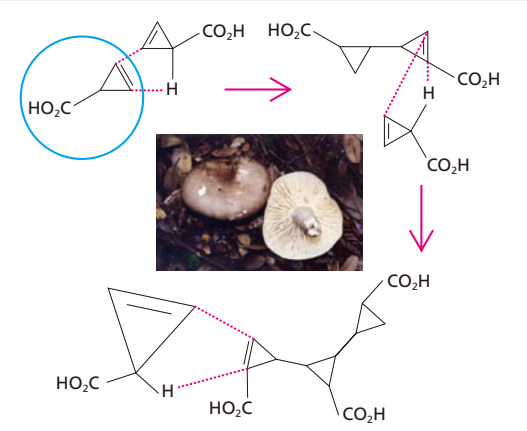
This achievement was the result of joint research with Dr. Kimiko Hashimoto (now Associate Professor at Kyoto Pharmaceutical University) as well as with Professor Masaya Nakata and Dr. Masanori Matsuura (then student) of the laboratory, to which Dr. Saikawa belongs. In the world of natural products investigation where almost all natural substances have been thoroughly investigated, this achievement has become a significant topic of conversation.

Toxic substance that disappears

Cycloprop-2-ene carboxylic acid is a small substance – a ring consisting of three carbon atoms, to which carboxylic acid is attached. "Such a simple, small substance has long been left unidentified!" Dr. Saikawa talks about the surprise that struck her after years of investigation.

Although its molecular structure is simple, its extraction was far from easy. The investigative study began with identification of the *Russula subnigricans* mushroom. To evaluate the toxicity, the team adopted the method of injecting the toxic substance into the peritoneal cavity of mice. But before long it became known that mice would die even when non-toxic substance was injected. So the experiment had to be done anew by changing the policy to feed mice with the toxic substance.

The hardest problem encountered was that the toxic substance would disappear when an ordinary separation process was employed. Looking back over those days, Dr. Saikawa says, "We tried this way, and if it didn't work we didn't hesitate to take that way. In that sense, research scientists like us are quick-tempered." The readiness to review and change research approaches as necessary and the toughness for devising and carrying out new solutions in rapid succession seem to be required. Finally, she found that the toxic substance disappeared due to concentration, which led to the improvement of the extraction process. Cycloprop-2-ene carboxylic acid was thus identified as the culprit for the *Russula subnigricans* mushroom after eight long years.



Cycloprop-2-ene carboxylic acid and polymerization

Russula subnigricans (photo) had been the only fatally poisonous mushroom the toxic component of which remained unidentified. But the lethally toxic component was finally identified as cycloprop-2-ene carboxylic acid (the blue-circled part in the upper left of the Fig.). When cycloprop-2-ene carboxylic acid molecules come closer to each other, polymerization takes place, which nullifies the toxicity. This explains why the toxicity disappeared during the concentration process of toxicity extraction. (Photo by Yoko Saikawa)

Scales falling from her eyes – an exciting moment!

"It was hard and depressing when positive results were not in sight. But the moment its structure was known, everything became clear and I found all answers just before my eyes." Once the structure of the toxic substance was identified, the question of the toxicity lost in the process of concentration was not a question at all. This excitingly fresh feeling derived from achievement seems to drive Dr. Saikawa into scientific pursuit. From this particular research project, she could also appreciate the joy of discovery of the natural world.

Discovery of new substances is also exciting as it allows her to pose new questions to other scientific fields. The greatest feature of this particular poison is that it causes "rhabdomyolysis" in which muscles melt. Since its mechanism remains totally unknown, the achievement of her team is now a focus of attention within medical circles.

I spare no trouble finding new seeds of research.

As a research scientist, Dr. Saikawa is about to launch a research theme on her own for the first time. In the past she frequented a zoo to sample hippopotamus sweat and climbed mountains many times in search of the targeted mushroom. From such experience she says, "Seeds of research themes are everywhere. But you can't find them if you're just sitting back watching TV or browsing through magazines. The only way is to use your own legs." To find new research themes, she often goes out to sea as early as 4:00 in the morning with a fisherman with whom she recently befriended.

(Reporter & text writer: Akiko Ikeda)