

## World's First Chemical Analysis Method Opens The Door To Faster Discovery Of Compounds With Possible Health Benefits

- A new method for isolating compounds and analyzing their structures at the molecular level quickly and efficiently that makes conventional methods obsolete
- Resolves manufacturing bottlenecks with a world-first discovery that connects research in food and medicine
- Winner of 2021 Hot Topics Award of the Japan Society for Bioscience, Biotechnology, and Agrochemistry

**TOKYO, Wednesday April 14, 2021** - Kirin Holdings Company, Limited (Kirin Holdings), the Kirin Central Research Institute (Central Research Institute, an R&D department), has established a world's first\*<sup>1</sup> analysis platform that swiftly separates individual compounds from investigated samples for analysis to quickly determine the structure of as yet unknown compounds\*<sup>2</sup>. This means that compounds can quickly be isolated into parts and structurally identified faster allowing for discovery of possible health benefits derived from those parts, as well as how to reproduce them. This method couples supercritical fluid chromatography\*<sup>3</sup> with the "crystalline sponge method" in cooperation with Kyowa Kirin Co., Ltd. (Kyowa Kirin) and added cooperation from an eminent scientist from the University of Tokyo. More on how this works below.

\*1 According to Kirin Holdings' research based on publicly available information as of March 18, 2021.

\*2 Reported at the [31<sup>st</sup> Conference of the Society for Chromatographic Sciences](#) (held at Shizuoka Prefecture Industry and Economy Assembly Hall from November 18 to 20, 2020)

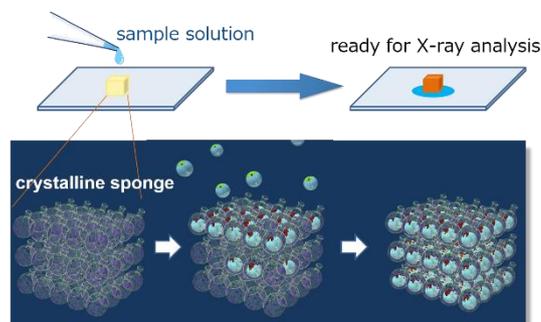
\*3 This is one way to purify or separate substances from a mixture for research. A feature of supercritical fluid chromatography is that it uses supercritical carbon dioxide and a trace amount of volatile organic solvent in the mobile phase. The small amount of organic solvent makes it an analysis technique with low environmental impact with excellent compound separation function.

Furthermore, Kirin Holdings has independently developed a technology to increase the versatility of the aforementioned analytical method. It accelerates the processes—such as the separation, isolation, and structure determination of compounds for analysis—that tend to act as bottlenecks in the course of research and development. This will realize gains such as the further optimization of the method to generate functional substances, even faster product development, and a more efficient production process. Kirin Holdings announced the research findings at the 2021 Annual Meeting of the [Japan Society for Bioscience, Biotechnology, and Agrochemistry](#) (JSBBA), held from March 18 to 21. These research findings were among 31 presentations selected from 1,299 general presentations applied to receive the Hot Topics Award.

### ● How it Works

A crystalline sponge is a porous single crystal with infinite pore channels with diameters of about 0.5 to 1 nanometer (1 nm = 1 billionth of a meter). The crystalline sponge method is a technology that enables the observation and determination of a compound's structure by soaking the crystalline sponge in a solution of the compound for analyzation of its molecular structure. This encases the compound in the pores, exposing it to X-rays and measuring the diffraction data.

Using the crystalline sponge method, the crystallization of the target compound, which had been considered essential in determining the structure of compounds under conventional X-ray analysis, is no longer necessary. In addition, since the structure of the compound can be observed using just a trace of a sample solution, the determination of the structure of a target compound—which is a bottleneck in current manufacturing—can be accelerated, garnering attention as a new technique for analyzing molecular structures.



## ● Background

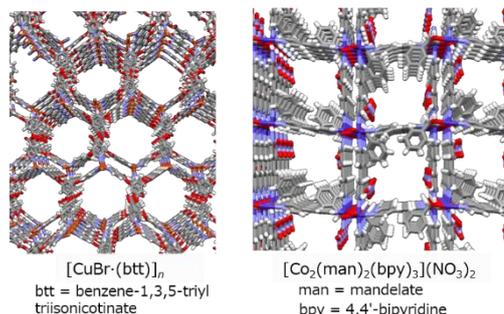
In food and pharmaceuticals, as well as various other fields of R&D, the separation of compounds in survey samples and the elucidation of their molecular structure is an important process. Since 2017, Kirin Holdings has participated in a social cooperation program established by Distinguished Professor Makoto Fujita at the Graduate School of Engineering, The University of Tokyo. Through open innovation, Kirin Holdings acquired the crystalline sponge method technology due to its innovative method of structural analysis. Furthermore, by coupling Kyowa Kirin's practical expertise in supercritical fluid chromatography coupled with the crystalline sponge method, Kirin Holdings developed an analytical platform that enables faster compound separation and structure determination. In addition, Kirin Holdings developed a technology that allows the use of multiple solvents to improve versatility. Normally, the type of solvents that could be used in this analytical method are limited.

## ● Outline

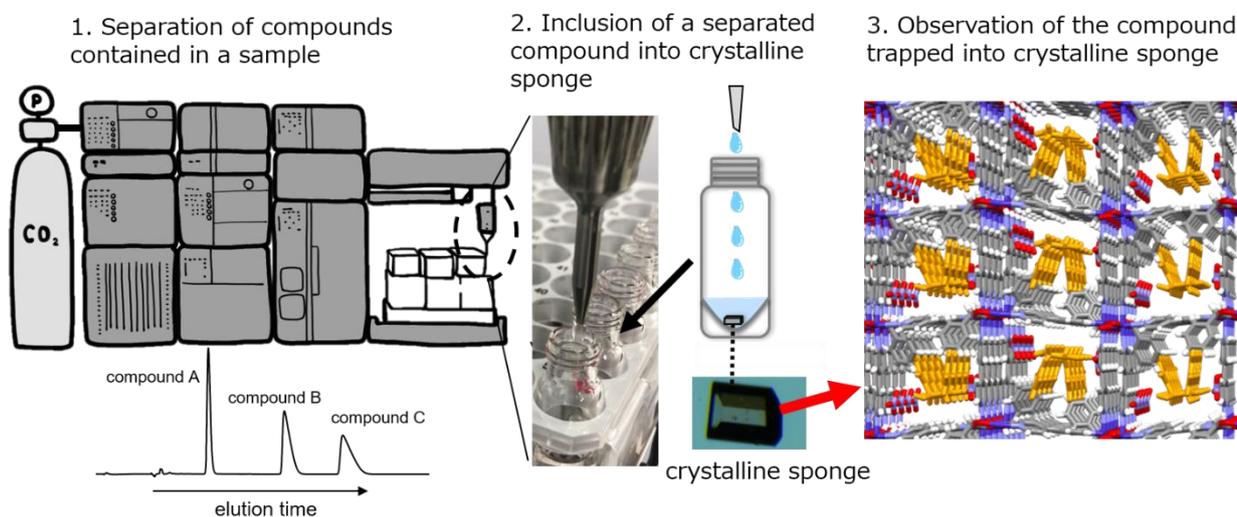
Previously, depending on the solvent, there had been an issue of the crystalline sponge being destroyed when it was soaked in solvent. Kirin Holdings focused on the resistance of the crystalline sponge to solvents as a limitation to this analytical method as a whole. In the process of seeking a crystalline sponge that is resistant to polar solvents\*4 like alcohol and acetonitrile, Kirin Holdings discovered a number of crystalline sponges that show resistance to polar solvents.

\*4 Indicates solvents with a high dielectric constant. In particular, it is easy for compounds like functional molecules, which are drug candidates, to dissolve in polar solvents, but many of these compounds hardly dissolve in non-polar solvents with low dielectric constants.

Polar solvent-resistant crystalline sponges discovered in this research



By utilizing these newly discovered crystalline sponges, it is now possible to analyze the compounds that were previously difficult to analyze using the crystalline sponge method. In addition, because a variety of solvents can now be used, the versatility of the analytical method is dramatically improved.



## ● Future Developments

With the establishment of its long-term management vision, Kirin Group Vision 2027, the Kirin Group aims to become a global leader in CSV,\*5 creating value across the world of Food & Beverages to Pharmaceuticals. To achieve that, as well as the existing businesses in the Food & Beverages domain and the Pharmaceuticals domain, the Kirin Group has established and growing its Health Science domain business in order to improve people's health based on the advanced fermentation and biotechnology techniques cultivated over many years,. In the Health Science domain, the Kirin Group is carrying out various R&D projects with emphasis on the areas of immunity, brain function, and the intestinal environment.

\*5 Creating Shared Value. Combined added value for consumers as well as for society at large.

Going forward, by applying this method as a basic technique to improve competitiveness in R&D in the Kirin Group's domains of Food, Pharmaceuticals, and Health Science, Kirin Holdings will accelerate its search for substances with as yet unknown health benefits. In addition, the process of developing new production and manufacturing methods will also be accelerated, aiming to create more products with added health benefits on an ongoing basis.

● **The Japan Society for Bioscience, Biotechnology, and Agrochemistry's Hot Topics Award**

[This award](#) is given to presentations judged to have academic and social impact announced at the annual meeting held by the JSBBA. It is a prestigious award given to about 30 presentations selected from registered presentations of general lectures. This new method was judged to have academic and social impact as a breakthrough in science with potential to accelerate the discovery of new functional ingredients. The award acknowledged the improved versatility of an analytical platform. This method will reap benefits such as the further optimization of substance generation methods for even faster product development, and a more efficient production process.

Notes

1. Title of presentation:  
Application of crystalline sponges resistant to polar solvents in supercritical fluid chromatography coupled to crystalline sponge x-ray analysis
2. Name of academic conference:  
2021 Annual Meeting of the Japan Society for Bioscience, Biotechnology, and Agrochemistry
3. Date of presentation:  
March 18-21, 2021
4. Presenters:  
Mayuka MIWA, Naoya KITADA, Yoshimasa TANIGUCHI, Kirin Central Research Institute, Research & Development Division, Kirin Holdings Company, Limited

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