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Amato Pharmaceutical Products, Ltd.

Mitsubishi Chemical Corporation

Amato Pharmaceutical Products and Mitsubishi Chemical found that the production of “butyric acid,” which plays a key role in improving the intestinal environment and promoting bowel movements, remarkably increases when prebiotics are combined with spore-forming lactic acid bacteria

-- Toward the strategic design of synbiotics leveraging the distinct properties of various prebiotics --

Amato Pharmaceutical Products, Ltd. (Head office: Toyonaka City, Osaka; President & CEO: Takashi Miyazaki) and Mitsubishi Chemical Corporation (Head office: Chiyoda-ku, Tokyo; President & CEO: Manabu Chikumoto) have confirmed that combining prebiotics[*1] such as oligosaccharides and dietary fiber with the probiotic[*2] spore-forming lactic acid bacterium *Heyndrickxia coagulans* SANK70258[*3] (hereinafter referred to as *Heyndrickxia coagulans*) (synbiotics[*4]) significantly increases butyric acid, which contributes to improving the intestinal environment and bowel movements. We both presented this study result at the 30th Annual Meeting of the Japanese Association for Dietary Fiber Research (October 18 and 19, 2025, in Hiroshima City, Japan).

This study demonstrated that various types of short-chain fatty acids[*5] are preferentially produced depending on the specific prebiotics used, and also revealed that even in cases where butyric acid production barely increased with prebiotics alone, it increases remarkably when used in combination with the probiotic *Heyndrickxia coagulans*. These results indicate that *Heyndrickxia coagulans* promotes the growth of butyrate-producing bacteria, thus leading to synergistic enhancement of the functional effects of the respective prebiotics. These results suggest that **combining the properties of “prebiotics and probiotics” (synbiotics) may enable the strategic design of a desirable intestinal environment (Fig. 1).**

The potential effects of prebiotics × Lacris™ on gut health improvement

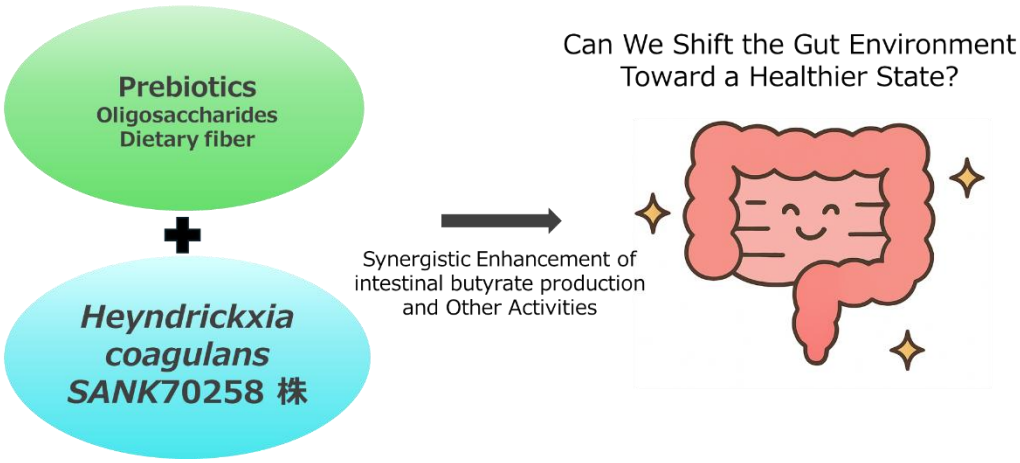

Fig. 1 Changes in the intestinal environment suggested due to the combination of prebiotics and probiotic *Heyndrickxia coagulans* (synbiotics)

Amato Pharmaceutical Products will leverage these findings to advance product development and information dissemination that supports intestinal health and improve bowel movements.

Mitsubishi Chemical will provide information regarding the design of synbiotics centered on the spore-forming lactic acid bacterium *Heyndrickxia coagulans* strain SANK70258 based on the insight obtained from this study, and will continue to pursue its scientific value and potential applications.

*1 Prebiotics

Refers to a food ingredient that improves the health of the host by increasing the growth or altering the activity of beneficial bacteria normally present in the digestive tract, or by otherwise exerting a beneficial effect on the host.

*2 Probiotics

Refers to live microorganisms that positively impact the health of the host by improving the balance of the intestinal flora.

*3 Spore-forming lactic acid *Heyndrickxia coagulans* SANK70258

Spore-forming lactic acid *Heyndrickxia coagulans* strain SANK70258, spore-forming lactic acid *Weizmannia coagulans* strain SANK70258, and *Bacillus coagulans* strain SANK70258 are the same strains.

*4 Synbiotics

Refers to a combination of probiotics and prebiotics. We aim to combine the two and promote the functions of both to produce a beneficial effect on health of the host.

*5 Short-chain fatty acids

Refers to organic acids containing six or fewer carbon atoms that are produced by intestinal bacteria. Examples include acetic acid, propionic acid, and butyric acid. They are produced when intestinal bacteria decompose dietary fiber. They are considered to contribute to growth suppression of harmful bacteria, promotion of peristalsis, and control of immune reaction by creating a slightly acidic intestinal environment.

■ Background

This study was a collaborative effort between Amato Pharmaceutical Products and Mitsubishi Chemical.

Based on the insights obtained through the sale of hemorrhoid medicines, Amato Pharmaceutical Products, which develops its BORRAGINOL® brand, produces products to prevent hemorrhoids and address lifestyle-related ailments under the “BORRA®” brand by focusing on three factors: “intestinal environment,” “bloodstream” and “cutaneous immunity,” all of which are known to cause hemorrhoids. The company is also engaged in development and sales of supplements and cosmetics. Mitsubishi Chemical aims to maximize the new functionalities of the spore-forming lactic acid bacteria *Heyndrickxia coagulans* strain SANK70258, in the field of well-being and improving the intestinal environment.

While pursuing the common goal of “improvement of the intestinal environment,” both companies have focused on “short-chain fatty acids,” which are known to play an important role in improving the intestinal environment and bowel movements. Among short-chain fatty acids, butyric acid in particular is difficult to produce because the proportion of butyrate-producing bacteria in the large intestine is relatively low. However, it is important as a major source of energy for intestinal epithelial cells and is thought to contribute greatly to improving the intestinal environment and bowel movements. It is believed that taking prebiotics and probiotics is effective in stably producing short-chain fatty acids in the intestines that have such improvement functions. However, the amount and pattern of production are affected by the type of prebiotics and concomitant use of probiotics (synbiotics). Therefore, in this study, we evaluated the difference in short-chain fatty acid production trends due to the use of prebiotics with different properties, as well as the effect on butyric acid production from the combination with *Heyndrickxia coagulans* strain SANK70258, a spore-forming lactic acid bacterium that can survive in gastric acid and reach the intestines while still viable.

■ Summary of the study

Purpose

Among the short-chain fatty acids produced in the large intestine, butyric acid is the

main energy source for intestinal epithelial cells and has multiple physiological functions, such as improving the intestinal environment and bowel movements, strengthening the intestinal barrier, and suppressing inflammation. In this study, we examined the effects of combining different prebiotics (lactulose [LAC], partially hydrolyzed guar gum [PHGG], isomaltodextrin [IMD], and beet fiber [BF]) with different properties with the spore-forming lactic acid bacterium *Heyndrickxia coagulans* strain SANK70258 [HC] on the production of short-chain fatty acids, particularly butyric acid.

Method

In vitro anaerobic culture tests were conducted using stool samples from 10 healthy Japanese subjects to measure short-chain fatty acid production and changes in the intestinal flora when each prebiotic was administered alone or in combination with HC.

Results

When prebiotics were used alone, different trends in short-chain fatty acid production were observed depending on the material used. Among the prebiotics used in the study, LAC was most likely to increase butyric acid production, while PHGG, IMD, and BF were most likely to increase the total amounts of acetic acid, propionic acid, and short-chain fatty acids. On the other hand, when HC was used in combination with each prebiotic, butyric acid concentrations increased compared to each prebiotic alone (Fig. 2).

When the intestinal bacteria were examined, it was found that butyric acid-producing bacteria (*Faecalibacterium*) in particular had increased. Furthermore, the combined use of PHGG or IMD with HC increased dietary fiber-decomposing bacteria (*Fusicatenibacter*).

These results suggest that HC may alter the composition of the intestinal microflora and shift the fermentation metabolic pathway of prebiotics to a "butyrate-dominant" type.

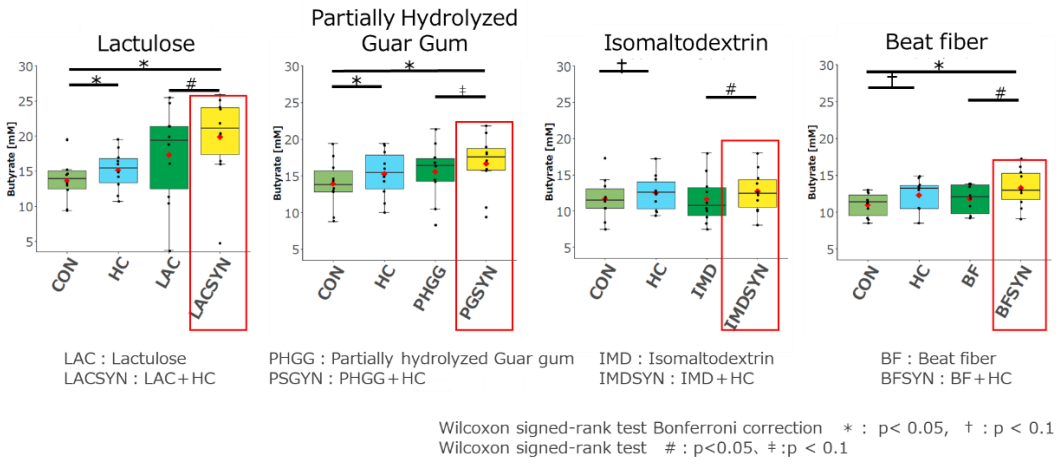

Fig. 2 Changes in butyric acid production by co-addition of each prebiotic and HC

■ **Conclusion**

In this study, we verified that (1) the types of short-chain fatty acids that are preferentially produced depend on the specific prebiotic; and (2) concomitant use of the spore-forming lactic acid bacterial strain *Heyndrickxia coagulans* SANK70258 remarkably increases production of butyric acid that is difficult to do using prebiotics alone.

These findings suggest that by combining the properties of prebiotics with the effects of probiotics, it may be possible to strategically design a desired intestinal environment (e.g., a butyrate-dominant type that improves bowel movements).

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