How dietary fiber and gut bacteria protect the cardiovascular system

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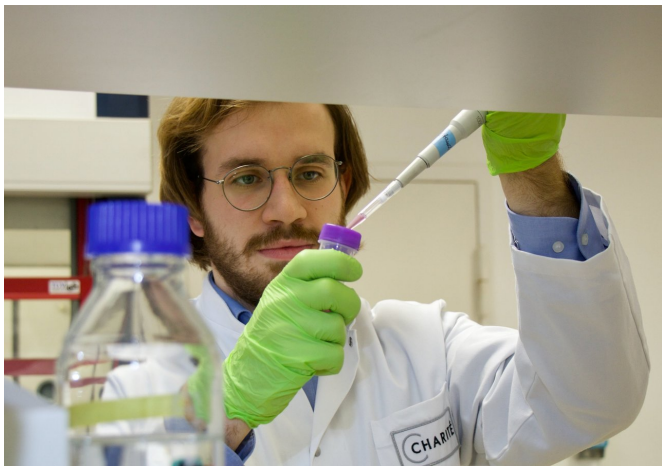

Hendrik Bartolomaeus in the lab. Credit: AG Müller, ECRC/MDC

The fatty acid propionate helps defend against the effects of high blood pressure, including atherosclerosis and heart tissue remodeling, a study on mice has found. Gut bacteria produce the substance—which calms the immune cells that drive up blood pressure—from natural dietary fiber.

"You are what you eat," as the proverb goes. But to a large extent our well-being also depends on what bacterial guests in our digestive tract consume. That's because gut flora help the human body to utilize food and produce essential micronutrients, including vitamins.

Beneficial gut microbes can produce metabolites from dietary fiber, including a fatty acid called propionate. This substance protects against the harmful consequences of high blood pressure. A Berlin research team from the Experimental and Clinical Research Center (ECRC), a joint institution of the Max Delbrück Center for Molecular Medicine (MDC) and Charité - Universitätsmedizin Berlin, shows why this is the case. Their study has been published in advance online in the journal *Circulation*.

The researchers fed propionate to mice with elevated blood pressure. Afterwards, the animals had less pronounced damage to the heart or abnormal enlargement of the organ, making them less susceptible to cardiac arrhythmia. Vascular damage, such as atherosclerosis, also decreased in mice. "Propionate works against a range of impairments in cardiovascular function caused by high blood pressure," says MDC researcher and research group leader Professor Dominik N. Müller. "This may be a promising treatment option, particularly for patients who have too little of this fatty acid."

Detour via the immune system

"Our study made it clear that the substance takes a detour via the immune system and thus affects the heart and blood vessels," say Dr. Nicola Wilck and Hendrik Bartolomaeus from the ECRC, who have been working together on the project for nearly five years. In particular, T helper cells, which enhance inflammatory processes and contribute to high blood pressure, were calmed.

This has a direct effect on the functional ability of the heart, for example. The research team triggered heart arrhythmia in 70 percent of the untreated mice through targeted electrical stimuli. However, only one-fifth of the animals treated with the fatty acid were susceptible to an irregular heartbeat. Further investigations with ultrasound, tissue sections, and single-cell analyses showed that propionate also reduced blood pressure-related damage to the animals' cardiovascular system, significantly increasing their survival rate.

But when researchers deactivated a certain T cell subtype in the mice's bodies, known as regulatory T cells, the positive effects of propionate disappeared. The immune cells are therefore

indispensable for the substance's beneficial effect. A research group under Johannes Stegbauer, an adjunct professor at Düsseldorf University Hospital, confirmed the team's findings in a second animal model.

Short-chain fatty acid as a therapeutic option

The results explain why a diet rich in fiber, which has been recommended by nutrition organizations for many years, helps prevent cardiovascular diseases. Whole-grain products and fruits, for example, contain cellulose and inulin fibers, from which gut bacteria produce the beneficial molecules like propionate, a short-chain fatty acid with a backbone of just three carbon atoms.

"Previously, it had not been clear which fatty acid is behind the positive effects and how it works," says Wilck. The study opens up new avenues in the treatment of cardiovascular diseases. "It might make sense to administer propionate or a chemical precursor directly as a drug—for example, when the blood of those affected contains too little of the substance.

Propionate still has to prove itself in everyday clinical practice. The research team now hopes to validate their findings by examining the substance's effects on human subjects. It is already known that propionate is safe for human consumption and can also be produced economically: The substance has been used for centuries as a preservative, for example. It is already approved as a food additive. "With these favorable conditions, hopefully propionate will soon make the leap from the lab to patients who need it," says Wilck.

More information: Hendrik Bartolomaeus et al. (2018): "The Short-Chain Fatty Acid Propionate Protects from Hypertensive Cardiovascular Damage." *Circulation*. DOI: 10.1161/CIRCULATIONAHA.118.036652

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