



Plain Language Summary

Can Citrate Help Prevent Calcium Buildup in PXE?

Plain language summary by Kanette Keough, PXE International Volunteer

Study at a Glance

Title: *ABCC6 and ANK regulate extracellular homeostasis of pyrophosphate and citrate and affect mineral deposition in bones and soft connective tissues*

Lead Institution: PXE International Center of Excellence in Research and Clinical Care, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania

Collaborating Institutions: HUN-REN Research Centre for Natural Sciences, Budapest, Hungary; and Labcorp, Morrisville, North Carolina

Study Type: Preclinical study using genetically altered mouse models of PXE

Citation: Szeri F, Niazi F, Ng C, Mikkelsen C, Rajpar I, Wu Q, Matyus SP, Connelly MA, Tavazze G, Lundkvist S, Tomlinson RE, van de Wetering K. *ABCC6 and ANK regulate extracellular homeostasis of pyrophosphate and citrate and affect mineral deposition in bones and soft connective tissues. bioRxiv [Preprint]. 2025 Oct 10:2025.10.09.681172. doi: 10.1101/2025.10.09.681172. PMID: 41279581; PMCID: PMC12632560.*

Summary: People with pseudoxanthoma elasticum (PXE) develop abnormal calcium buildup in places where it shouldn't occur, including the skin, eyes, and blood vessels. Scientists already know that people with PXE have lower levels of inorganic pyrophosphate, a natural substance that helps prevent calcium from building up in soft tissues. A recent study asked whether another naturally occurring substance, citrate, might also help protect the body.

Researchers studied specially bred mice that develop many of the same calcium buildup problems seen in people with PXE. Some mice lacked a working *ABCC6* gene, the gene responsible for PXE in people, while others carried a mutation in the *ANK* gene, which helps regulate mineral balance. The researchers also studied mice with changes in both

genes. They found that mice without a working *ABCC6* gene had lower pyrophosphate levels, while mice with variants in the *ANK* gene had much lower citrate levels. Mice with changes in both genes developed the most severe calcium buildup.

The researchers also found that high doses of oral citrate reduced calcium buildup in the PXE mouse model. These findings suggest that citrate may help protect the body through a pathway that is different from pyrophosphate. The study also highlighted ANK as another important pathway that scientists may explore as they search for new treatments.

Although these results are encouraging, this research was conducted only in mice. It does not show that citrate supplements prevent or treat PXE in people, and the doses used in the study cannot be directly applied to patients. More research, including studies in humans, will be needed before doctors know whether citrate could become part of future treatment.

Studies like this help scientists better understand why calcium builds up in PXE and identify new ideas that may eventually lead to better treatments. While this research does not change current medical care, it provides another promising direction for scientists working to improve the lives of people living with PXE.

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