A dietary supplement bodybuilders use to bulk up may have a more sweeping health benefit: Staving off the ravages of old age. Mice given the substance—alpha-ketoglutarate (AKG)—were healthier as they aged, and females lived longer than mice not on the supplement.

Other compounds, like the antiaging drug rapamycin and the diabetes treatment metformin, have shown similar effects in mouse experiments. But AKG is naturally made by mice and by our own bodies, and it is already considered safe to consume by regulators.
“The big thing about this is that its safety profile is so good,” says University of North Dakota aging researcher Holly Brown-Borg, who was not involved with the study. “It has potential and should be explored further, for sure.”

AKG is part of the metabolic cycle that our cells use to make energy from food. In addition to its use by bodybuilders, doctors sometimes treat osteoporosis and kidney disease with the supplement.

The molecule grabbed attention as a possible antiaging treatment in 2014, when researchers reported AKG could extend life span by more than 50% in tiny Caenorhabditis elegans worms. That’s on par with a low-calorie diet, which has been shown to promote healthy aging, but is hard for most people to stick with. Other groups later showed life span improvements from AKG in fruit flies.

In the new study, Gordon Lithgow and Brian Kennedy of the Buck Institute for Research on Aging and colleagues turned to mammals. They gave groups of 18-month-old mice (about age 55 in human years) the equivalent of 2% of their daily chow as AKG until they died, or for up to 21 months. AKG levels in blood gradually drop with age, and the scientists’ aim was to restore levels to those seen in young animals.

Some differences jumped out within a few months: “They looked much blacker, shinier, and younger” than control mice, says Azar Asadi Shahmirzadi, a postdoc at the Buck Institute who did the experiments as a graduate student. In addition, the AKG-fed mice scored an average of more than 40% better on tests of “frailty,” as measured by 31 physiological attributes including hair color, hearing, walking gait, and grip strength. And female mice lived a median of 8% to 20% longer after AKG treatment began than control mice, the group reports today in Cell Metabolism.

The AKG-eating mice did not perform better on tests of heart function or treadmill endurance, however, and the tests did not include cognitive performance.

Probing the mechanism for these improvements, the researchers found that female mice receiving AKG produced higher levels of a molecule that tamps down on inflammation. Chronic inflammation can spur many diseases of aging such as cancer, heart disease, arthritis, and dementia.
The effects on life span and health were smaller for AKG than for some other antiaging compounds, notes aging researcher Matt Kaeberlein of the University of Washington, Seattle, who was not involved with the work. But some of those compounds have run into safety issues—for example, rapamycin suppresses the immune system and may promote diabetes.

Kennedy, now also at the National University of Singapore, plans to test AKG in human volunteers soon. Looking at a group of people between the ages of 45 and 65, his group will see whether the molecule improves aging-related biomarkers such as inflammation, arterial hardening, and a type of chemical signature on DNA associated with aging. The company Ponce de Leon Health, where Kennedy serves as chief scientific officer (and Gordon and other paper authors have stock), is running a similar study at Indiana University.

Ponce de Leon Health already sells a formulation of AKG called Rejuvant that it says can “slow the aging process.” Kennedy defends these claims. “We are upfront about the data that we have and do not yet have on the website,” he says. And Brown-Borg notes the Buck Institute team isn’t the first group of aging-focused researchers to start a company to develop an antiaging treatment, an idea she hopes will eventually pan out in clinical trials. “It’s an exciting time in the field,” she says.