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Natural compound from green tomatoes stimulates muscle growth, improves muscle strength and endurance

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As unlikely as it sounds, green tomatoes may hold the answer to bigger, stronger muscles. Using a screening method that previously identified a compound in apple peel as a muscle-boosting agent, a team of University of Iowa scientists has now discovered that tomatidine, a compound from green tomatoes, is even more potent for building muscle and protecting against muscle atrophy.

Muscle atrophy, or wasting, is caused by aging and a variety of illnesses and injuries, including cancer, heart failure, and orthopedic injuries, to name a few. It makes people weak and fatigued, impairs physical activity and quality of life, and predisposes people to falls and fractures. The condition affects more than 50 million Americans annually, including 30 million people over age 60, and often forces people into nursing homes or rehabilitation facilities.

"Muscle atrophy causes many problems for people, their families, and the health care system in general," says Christopher Adams, M.D., Ph.D., UI associate professor of internal medicine and molecular physiology and biophysics. "However, we lack an effective way to prevent or treat it. Exercise certainly helps, but it's not enough and not very possible for many people who are ill or injured."

More muscle, less fat

In a new study, published online April 9 in the *Journal of Biological Chemistry*, Adams searched for a small molecule compound that might be used to treat muscle atrophy. He zeroed in on tomatidine using a systems biology tool called the Connectivity Map, which was developed at the Broad Institute of MIT and Harvard University. Adams discovered that tomatidine generates changes in gene expression that are essentially opposite to the changes that occur in muscle cells when people are affected by muscle atrophy.

After identifying tomatidine, Adams and his team tested its effects on skeletal muscle. They first discovered that tomatidine stimulates growth of cultured muscle cells from humans.

"That result was important because we are looking for something that can help people," Adams says.

Their next step was to add tomatidine to the diet of mice. They found that healthy mice supplemented with tomatidine grew bigger muscles, became stronger and could exercise longer. And, most importantly, they found that tomatidine prevented and treated muscle atrophy.

Interestingly, although mice fed tomatidine had larger muscles, their overall body weight did not change due to a corresponding loss of fat, suggesting that the compound may also have potential for treating obesity.

Designing healthier foods

An attractive aspect of tomatidine is that it is a natural compound derived from tomatoes. It is produced when alpha-tomatine, which is found in tomato plants and in green tomatoes in particular, is digested in the gut.

"Green tomatoes are safe to eat in moderation. But we don't know how many green tomatoes a person would need to eat to get a dose of tomatidine similar to what we gave the mice. We also don't know if such a dose of tomatidine will be safe for people, or if it will have the same effect in people as it does in mice," Adams says. "We are working hard to answer these questions, hoping to find relatively simple ways that people can maintain muscle mass and function, or if necessary, regain it."

Adams and his team previously used this same research strategy to discover that ursolic acid, a compound from apple peels, promotes muscle growth.

"Tomatidine is significantly more potent than ursolic acid and appears to have a different mechanism of action. This is a step in the right direction," Adams says. "We are now very interested in the possibility that several food-based natural compounds such as tomatidine and ursolic acid might someday be combined into science-based supplements, or even simply incorporated into everyday foods to make them healthier."

In an effort to accelerate this research and translate it to people, Adams and his colleagues have founded a biotech company called Emmyon. The company recently received funding from the National Institutes of Health to develop strategies for preserving muscle mass and function during the aging process. The company is also using tomatidine and ursolic acid as natural leads for new medicines targeting muscle atrophy and obesity.

More information: www.jbc.org/content/early/2014 … 556241.full.pdf+html