Apple peel makes mice mighty

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For Popeye, spinach was the key to extra muscle. For the mice in a new University of Iowa study, it was apples, or more precisely a waxy substance called ursolic acid that's found in apple peel.

The UI study, published in the June 8 issue of the journal Cell Metabolism, showed that ursolic acid reduced muscle atrophy (also known as muscle wasting) and promoted muscle growth in mice. It also reduced fat, blood sugar levels, cholesterol and triglycerides in the animals. The findings suggest that the compound may be useful for treating muscle wasting and possibly metabolic disorders such as diabetes.

"Muscle atrophy causes big problems. It's also very common -- it affects most people at some point in their lives, during illness or aging. But, there's no medicine for it," said Christopher Adams, M.D., Ph.D., UI endocrinologist and senior author of the study. "We studied muscle gene activity in people with atrophy and used that information to find chemicals that might block atrophy. One of those chemicals was especially interesting. It's called ursolic acid and it's particularly concentrated in apple peels.

"The old saying goes that 'an apple a day keeps the doctor away.' So, we tested ursolic acid in mice, and found that it increased the size and strength of their muscles," Adams added. "It did this by helping two hormones that build muscle: insulin-like growth factor-1 (IGF1) and insulin. Because ursolic acid increased muscle, it reduced muscle atrophy. Surprisingly, it had some other beneficial effects in mice: for

example, it reduced body fat, and lowered blood glucose and cholesterol."

Adams and colleagues homed in on ursolic acid by using connectivity maps, a relatively new technique that compares gene expression patterns in cells under different conditions. The team determined which genes are turned on or off in human muscle during atrophy and compared that pattern with gene expression patterns in cultured cell lines treated with a library of different compounds. They discovered that one of those compounds -- ursolic acid -- causes a pattern of gene expression that is the opposite of the pattern caused by atrophy. This suggested that ursolic acid might reverse atrophy.

In follow-up experiments, the researchers proved that mice fed ursolic acid were indeed protected from muscle atrophy caused by both fasting and nerve damage. Furthermore, healthy mice fed ursolic acid developed larger, stronger muscles than mice that did not receive the compound.

The study suggests that ursolic acid's ability to both inhibit muscle wasting and promote muscle growth stems from its ability to influence IGF1. This hormone, and its close cousin insulin, both bind to receptors on muscle cells setting off a cascade of cellular pathways that either enhance muscle growth or block atrophy. Ursolic acid appears to increase the activity of the receptors for IGF1 and insulin, amplifying the beneficial effects of these hormones in muscle.

Interestingly, although ursolic acid increased muscle weight in mice, it did not increase total body weight, and further investigation showed that mice fed ursolic acid had less body fat than mice that were not fed the compound.

Adams and his colleagues now hope to move the research toward human trials.

Provided by University of Iowa