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## Red Wine Compound Promises Longevity, Study Finds

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A substance found in red wine protected mice from the ill effects of obesity, raising the tantalizing prospect the compound could do the same for humans and may also help people live longer, healthier lives, researchers are reporting today. .

The substance, called resveratrol, enabled mice that were fed a high-calorie, high-fat diet to live normal, active lives despite becoming obese -- the first time any compound has been shown to do that. Tests found the agent activated a host of genes that protect against the effects of aging, essentially neutralizing the adverse effects of a bad diet on the animals' health and lifespan.

Although much more work is needed to explore the benefits and safety of the substance, which is sold over the counter as a nutritional supplement, the findings could lead to the long-sought goal of extending the healthy human lifespan, experts said. Preliminary tests in people are already underway.

"We've been looking for something like this for the last 100,000 years, and maybe it's right around the corner - a molecule that could be taken in a single pill to delay the diseases of aging and keep you healthier as you grow old," said David A. Sinclair, a Harvard University molecular biologist who led the study. "The potential impact would be huge."

The findings triggered excitement among scientists studying aging, who hailed the findings as groundbreaking.

"This represents a likely major landmark," said Stephen L. Helfand, who studies the molecular genetics of aging at Brown University. "This really pushes the field forward. It's quite exciting."

The research, being published in tomorrow's issue of the journal *Nature*, helps explain a host of observations that have long intrigued researchers, including why French people tend to get fewer heart attacks and why severely restricting the amount of calories animals ingest makes them live longer.

"This gives us hope that the idea of harnessing the power of calorie restriction is not a fantasy and can be brought to reality," said Leonard Guarente, who studies the biology of aging at the Massachusetts Institute of Technology. "This could produce a whole new approach to preventing and treating the diseases of aging."

Previous research has shown that laboratory animals fed very low-calorie diets live significantly longer, which has prompted some people to try strenuous "caloric restriction" diets as a possible fountain of youth, even though its effectiveness in humans remains unproven.

In the hope of finding a drug that could harness the natural life-extending capabilities activated by caloric restriction, Sinclair and his colleagues identified a number of promising compounds, including resveratrol, which is found in red wine, grape skins and other plants. The compound, which increases the activity of

enzymes known as sirtuins, prolonged the lifespan of every organism scientists have tested it on, including yeast, worms, fish and fruit flies.

To examine for the first time whether resveratrol could also extend longevity in mammals, Sinclair and his colleagues studied year-old mice, which are the equivalent of middle-aged humans. One third of the mice were fed a standard diet. Another third ate the equivalent of a junk-food diet -- one very high in calories with 60 percent of the calories coming from fat. The last third lived on the unhealthy diet combined with resveratrol.

After a year, the researchers found that both groups of mice that ate the junk food diet got fat, and those that did not get any resveratrol experienced a host of health problems, including the early signs of diabetes and heart disease. They tended to die prematurely.

But the mice that got resveratrol remained healthy and lived as long as the animals that ate a normal diet and stayed thin -- adding the equivalent of about 10 or 20 human years to their lifespan. Moreover, the hearts and livers of the animals getting resveratrol looked healthy, the activity of a host of key genes appeared normal and they showed some of the biological changes triggered by caloric restriction. They also appeared to have a better quality of life, retaining their activity levels and agility.

"It is really quite amazing," Sinclair said. "The mice were still fat but they looked just as healthy as the lean animals."

The researchers cautioned that the findings should not encourage people to eat badly, thinking resveratrol could make gluttony completely safe. They also noted that a person would have to drink at least 100 glasses of red wine a day or take mega doses of the commercially available supplements to get the levels given to the mice, which may not be safe in humans.

But the findings indicate that resveratrol or molecules like it could have myriad benefits, and several aging researchers said the results tempted them to start using the supplements in the meantime.

"I'm usually a very cautious person," said Cynthia Kenyon of the University of California in San Francisco. "But I'm seriously thinking about taking resveratrol myself. It seems pretty wonderful."

"I actually told my mother she should take it," Helfand said. "I even went out and got her some."

The researchers are continuing to study the remaining living mice to gauge the full benefits, as well as other mice fed a normal diet or a calorie-restricted diet along with resveratrol to see whether the substance extends life in non-obese animals. So far the results appear promising, researchers said.

"This appears to have a lot of potential," said Rafael de Cabo of the National Institute on Aging, which helped conduct and fund the study.

Sirtris Pharmaceuticals, a Cambridge, Mass., biotech company that Sinclair helped start and that helped fund the mouse study, has already begun testing a version of resveratrol on diabetic humans. Other companies are studying similar substances.

"For now, we counsel patience," wrote Matt Kaeberlein and Peter S. Rabinovitch of the University of Washington in an article accompanying the study. "Just sit back and relax with a glass of red wine . . . if you must have a Big Mac, fries and apple pie, we may soon know if you should supersize that resveratrol shake."

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