



## Resveratrol In the News

## 60 Minutes Report

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# Fountain of Youth in a Wine Rx?

## Researchers Tell Morley Safer Red Wine Substance Resveratrol Could One Day Lengthen Lives

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Eighteen years ago, *60 Minutes* first examined the so-called French paradox, which suggested that the French - despite a high fat diet and high consumption of wine - had a remarkably low incidence of heart disease compared with Americans. Most researchers agreed that there was something in the wine that offered protection, and a few years later, even the highly cautious federal dietary guidelines say that moderate consumption of red wine can be beneficial.

As *60 Minutes* reported in January, scientists across the country have identified a substance in red wine called **resveratrol** that they believe might do more than just protect the heart, but could in very high concentrations significantly extend life by preventing a number of age related illnesses.

If they're right, we all may soon be taking a pill that could give us an extra decade or two of healthy old age.

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"If the promise holds true, I think this has the chance to change healthcare," Dr. Christoph Westphal tells **correspondent Morley Safer**.

Dr. Westphal says we all may soon be taking a drug that just might beat the clock, a simple pill that could delay the inevitable. "Our goal is to prevent and forestall many of the diseases that strike us as we reach 50, 60, and 70. All with one pill."

Asked if he's suggesting that it's some kind of a rejuvenation drug that would turn a 70-year-old into a 35-year-old, Westphal tells Safer, "That might be pretty hard to do. But I think if we're on a train heading one direction, we can slow down that train. I think we can slow down these genes that control the aging process."

That quest to put death on hold began in 2003 when Westphal met David Sinclair, a biochemist at Harvard who was studying the genetic components of aging. "Five years ago I met David. And he had shown that you could extend life span in yeast. That's pretty exciting," Westphal recalls.

Yeasts are one thing, human beings are more complicated. So Sinclair focused on a gene present in almost all life forms: the sirtuin gene (sirt 1). It's normally inactive, but when it is active, Sinclair believes it triggers a survival mechanism that extends life. Convinced that something in nature could activate that gene, Sinclair randomly tested thousands of compounds and got a hit: **resveratrol**.

"When I Googled this resveratrol, I was shocked to find that red wine was the top hit," Sinclair remembers.

Red wine is brimming with resveratrol. It is found in high concentrations in the skin of the grape, and seems to play a role in protecting it from invading bacteria and fungi.

Sinclair says he was aware of research into red wine and certain health benefits. "I mean, that's why I almost fell off my chair when the link was made. And I thought that this was a potential explanation for the benefits of red wine."

The important news here is not that we'd found something in red wine. The important thing is that we passed a milestone where we can now make drugs based on this knowledge and we can potentially slow down aging itself," Sinclair explains.

Everyone from plastic surgeons to your friendly snake oil salesman have been promising a ticket to eternal youth for some time, so the prospect of a pill based on red wine that could trigger a longevity gene sounds too good to be true. And yet scientists have actually known for years of one surefire of doing that: stay hungry.

"Eating a lot of food turns that off. Dieting, extreme dieting turns it on," Sinclair says.

In one experiment, a group of rhesus monkeys is on a major diet. For nearly two decades

they have been taking in a good 30 percent fewer calories than their well-fed brothers and sisters.

They are the centerpiece of a National Institutes of Health study at the University of Wisconsin on whether or not CR- calorie restriction - makes them healthier and extends their lives. To maintain their sterile environment, the **60 Minutes** team had to suit up to visit them with Ricki Colman, the "project leader."

The control animals are nearing the end of a typical monkey lifespan, about 27 years, and major differences in their overall health are becoming clear. The skinny monkeys actually look younger, their coats are shinier, and fewer have arthritis.

And the chunky monkeys? Many have diabetes, and a significantly higher number have cancer and heart disease.

Pound for pound, Colman says the lighter monkeys do better. **(CBS)** Dr. Richard Weindruch, who heads up the study, believes that calorie restriction turns on these monkeys' genetic survival switch. A hungry life seems to lead to a longer life.

"There is an emerging survival advantage for the monkeys on caloric restriction and 50 percent of the normally-fed animals have died. And maybe 25 percent of those on caloric restriction," Dr. Weindruch explains.

"That's a pretty remarkable number. Surely those are strong indications that restricted calorie intake among humans would be extremely beneficial," Safer remarks.

"It appears to support that idea," Weindruch agrees.

But our record as humans staying on diets is pretty miserable and worsening. So it's a fat chance that we'll all be giving up our passion for greasy junk. We consume tons more calories than we need but, believe it or not, there are some Americans who just revel in their hunger.

Meet the members of CRS - the Calorie Restriction Society - a group that has been severely restricting their calories for years now. They are also part of a Washington University study to see if humans "mimic" the monkeys. Does this kind of self-denial makes them live longer, healthier lives?

**60 Minutes** joined them for what they call "happy hour," consisting of a cocktail of low-calorie soup for starters, and walnuts, and baby food - green bean puree on flour-free bread to top off this feast fit for a flea.

So far the participants have lowered their blood pressure, reduced body fat, and lessened risk factors for heart disease, diabetes and even cancer. And what's more, to one husband anyway, starvation has its sexy side. "To be honest, if you saw her without any clothes, you'd see she looks pretty darn good, like a woman like of many, many years younger,"

the man told *60 Minutes*.

Their emissaries travel the world, spreading the faith and the word: hunger turns on the survival gene.

The skinnies may not die young, but given their diet they just might die of boredom. But if the scientists are on the right track, it could mean forget dieting, forget the sweaty business of working out - just pop a pill and you are in guilt-free couch potato paradise.

**(CBS)** "We have a pill that can mimic many of the effects of calorie restriction or exercise," Westphal says.

"So one could be very healthy and obese at the same time," Safer remarks.

"Our goal is healthy individuals, ideally via lifestyle, and if that doesn't work, we believe that we'll have a pill that can mimic that," Westphal replies.

A pill that - in effect - diets for you, a pill that turns on the survival gene.

"What we're trying to do is to put the body in a defensive state to ring the alarm bells and get the body to defend itself instead of dieting to set the alarm off, pop a pill," Sinclair says.

The pill a form of resveratrol, a virtual vineyard of healthy living. Asked how much red wine one would have to drink to get the kind of resveratrol they are using in their experimental pills, Sinclair says, "Well, the sad news is that you'd need to drink about 1,000 bottles a day of red wine, which I don't recommend."

Resveratrol itself may not extend lifespan but could prevent the diseases of aging, like Alzheimer's, diabetes, heart disease, even cancer. "What we're talking about is activating the body's natural, genetic defenses against diseases. And that's very powerful if we can harness that," Sinclair says.

Resveratrol has been tested on mice and the results have been encouraging. In a test-video provided, two mice were fed a high fat diet for 12 weeks. But when placed on a treadmill, one mouse ran twice as far. He was given high concentrations of resveratrol.

"You have fat mice, and you have fat mice with resveratrol. And the ones that are on resveratrol, they can run twice as far, and they live longer, about 20 percent longer," Sinclair says.

Other studies showed that among mice fed a high fat diet, those taking resveratrol didn't gain as much weight as those not given the drug. Sinclair believes that resveratrol actually changes the physiology of the mice.

The proof, he says, is in the post-mortems. "Their organs looked pristine, youthful, fat-

free, and their physiology was just like they were dieting. But they were fat."

Convinced that they were on the right path, they fast-tracked into human trials on people with untreated diabetes. The results were impressive: it significantly lowered glucose and insulin levels, without the patients changing their diet or taking any other drugs.

"Originally our hope was that you'd be able to prevent diseases of aging. What we ended up seeing is actually you could therapeutically intervene in patients who have diseases of aging. And that was unexpected," Westphal says.

"Yeah, the diabetic patients with high blood sugar, and the molecules bring it down. That's treatment. That's not prevention," Sinclair adds.

**CBS)** These scientist are now developing what they say is a much more potent synthetic version of resveratrol that will also soon go into human trials, this time on cancer patients.

"I keep on thinking, you know, what used to seem like it was science fiction, I actually believe the biology is right. And if we're right this may be the most important thing that we're going to do in our live," Westphal says.

Still, the speed and results of resveratrol are unusual, and Sinclair believes it will not only keep people living longer, but will keep them healthy longer. "We're talking about is potentially making a 90-year-old as healthy as a 60-year-old. A 90-year-old can play tennis, and see their great grandkids graduate from college. People will live active, healthy lives and then die quietly in their sleep. And that's really the aim here with this," he says.

Asked if humans are on the edge of maintaining lives into their 100s, Sinclair says, "Well, we certainly passed a corner in terms of the science. And someone's going to achieve it. And if it's not us, it's gonna be someone else."

But the question that most of us want answered is: will this happen within our lifetimes. I'm fairly certain about that," Sinclair says.

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Initial test results on cancer patients are expected this September. Last summer, Dr. Sinclair and Dr. Westphal's little start-up company was bought by the pharmaceutical giant GlaxoSmithKline for almost three quarters of a billion dollars.