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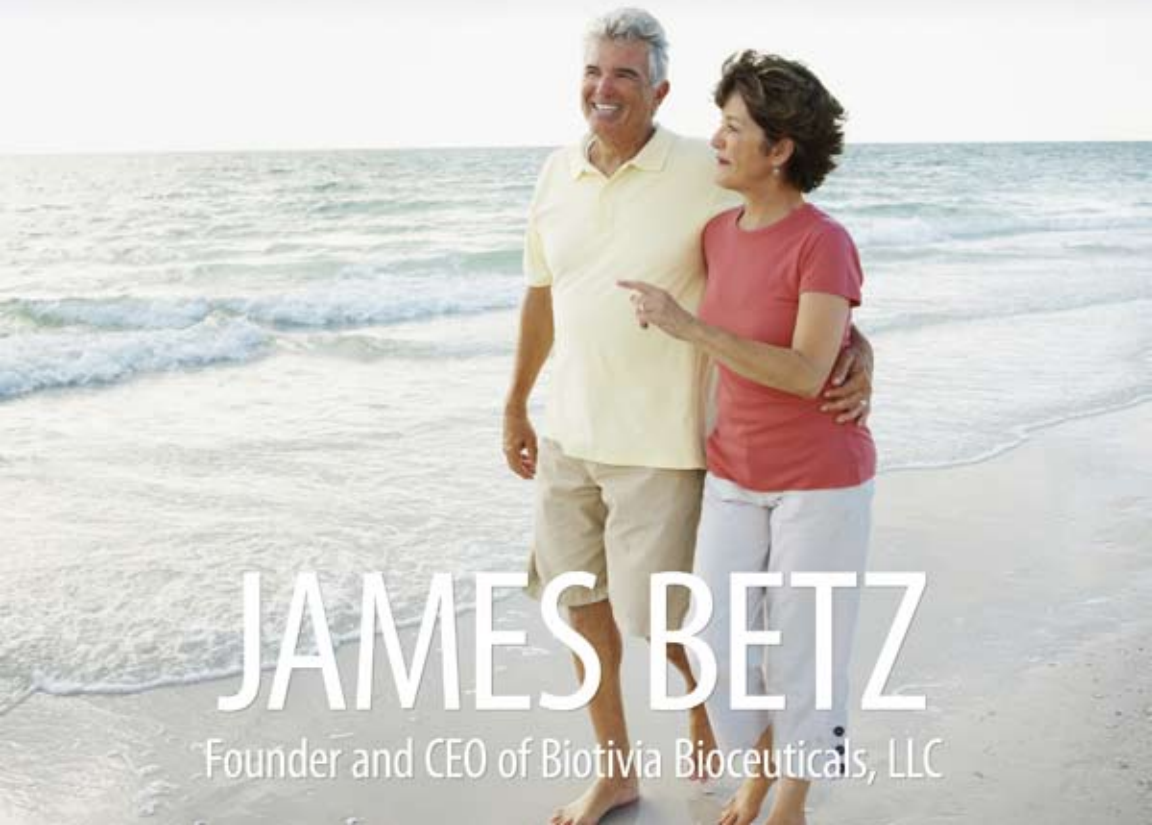
and its Effects on Human Health and Longevity - Myth or Miracle?



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Introduction

Is resveratrol, as many scientists believe, a breakthrough discovery destined to make a greater contribution to human health and the prevention and treatment of age-related disease than antibiotics; or is it only another false promise which is taking scarce research dollars and talent away from the development of pharmaceuticals the world needs now to treat an aging population?

With obesity, diabetes, coronary disease, Alzheimer's disease and cancer reaching near pandemic levels in the developed world, surely a compound with the putative disease prevention and treatment powers of resveratrol cannot be dismissed without extensive scientific investigation. Only five years ago physicians, scientists and pharmaceutical companies had barely heard of this natural compound, and only a handful of scientists and physicians possessed any real knowledge of the molecule's potential health and wellness effects.

The first high-strength resveratrol supplement, Bioforte, was not even on the consumers' radar. A few animal studies had shown the potential for increases in life span, and a few hundred investigations—primarily by researchers at universities in Japan, India and China—elucidated resveratrol's chemoprotective properties, particularly with respect to cancer and diabetes. However, the same could be said for hundreds of other phytochemicals and synthetic drugs that had at one time or another shown promising results in the lab, only to be shuttled off to oblivion when scientists were unable to replicate the same effects in mammals, especially humans.

One intriguing and rather unique aspect of resveratrol that caught the attention of both researchers and the public was its ability to extend

the lifespan of some animals. Fish fed resveratrol, for example, lived 59 percent longer than the same species without resveratrol. Obese mice lived 31 percent longer and managed to avoid all of the diseases normally associated with aging and obesity.

The big missing element in the resveratrol equation, however, was a lack of published human clinical trials by major medical schools and research institutions. Very little was then known also about the potential toxicity of resveratrol in humans or what might constitute a correct dose; and there were concerns about the low bioavailability of resveratrol, as well as questions about its possible estrogenic effects. Some scientists speculated that women might be best advised to avoid resveratrol for this reason. We now know that precisely the opposite is true. Resveratrol has been shown in a wealth of studies to be a powerful chemoprotectorant and chemotherapeutic agent against breast cancer. It seems that, as more resources are devoted to the study of this potent molecule, new medical and quality of life applications come to light on a regular basis.

As the results of the earlier studies were successfully replicated, and new investigations by research teams around the world uncovered a virtual laundry list of critical transcription factors, signaling pathways and other important pharmacokinetic effects of this very small molecule, interest in resveratrol increased exponentially in Asia, the US and Europe. By late 2010, there were over 4,000 published studies on resveratrol and a remarkable consensus was developing. Not only were scientists finding unusually consistent and replicable positive results, as one institution after the other examined the molecule using different approaches and technologies, but fundamental new effects and modes of action were being discovered at an astonishing rate. Many of these diverse properties of resveratrol have potentially huge implications for the prevention and treatment of human disease.

Only time will tell if resveratrol manages to unseat antibiotics to take the top spot as the most important contributor to human health, but at this point in time it cannot be counted out. In terms of its beneficial properties relative to chronic conditions such as diabetes, cardiovascular diseases, many cancers and fitness, resveratrol is a strong contender—and for resveratrol the race has just begun.

Resveratrol versus penicillin

In an interview with a well-known international technology magazine in March 2009, I told the journalist; "In my opinion, resveratrol will, in the space of 20 or 30 years, come to be regarded as a more important scientific development than penicillin." In this prediction I was referring to this small molecule's potential to positively impact the health, longevity, and quality of life of the human race. Seven months after my interview, a scientist researching resveratrol at Harvard University took this prediction one step further by proclaiming that resveratrol will be more important than all antibiotics.

Penicillin was discovered in 1928 and has been credited with saving many thousands, if not millions, of lives. Resveratrol was first isolated from a plant source in 1940 in the West, but has been used as a traditional medicine in Asia for more than 2,000 years. In 1970 it was first characterized as a chemopreventive, a substance that protects healthy human tissue from the disease-causing effects of various agents such as poor diet, bacteria, viruses and aging. An example of a chemopreventive would be the use of low dose aspirin to protect against heart attacks.

Both penicillin and resveratrol, like most drugs with a long history of efficacy, are derived from natural sources; penicillin comes from a common fungus, and resveratrol is found in a variety of plants including grapes,

peanuts and cranberries, but most importantly in the Japanese Giant Knotweed plant, also known as Polygonum-cuspidatum. Giant knotweed has been used in Asia as a traditional medicine to treat immune disorders, cancer, and neurological conditions. The plant acquired a rather unsavory reputation as a foreign invader throughout Southeast Asia and Japan, owing to its ability to survive in the harshest conditions and to crowd out other plants and crops. Five years ago a Google search for giant knotweed would return hundreds of articles on how to exterminate it. The same search today would be filled with scientific studies elucidating its astonishing medical and health applications.

The scientific community recognizes resveratrol's potential

In September 2010 the first international conference of resveratrol researchers was held about a one-hour train ride outside of Copenhagen, Denmark. At this milestone event, over 120 of the world's leading scientists from prestigious research institutions in the US, Asia, India, Europe and Australia met to present their findings on resveratrol. After attending this conference and listening to the presentations of these distinguished and highly accomplished scientists, I am now convinced that, if anything, my comparison of resveratrol with penicillin was extremely conservative.

Resveratrol and the drugs, treatments, supplements and functional foods that contain this tiny but incredibly potent molecule, will eclipse penicillin's importance within one generation. From 1940 until 2005, there were some 800 published studies on resveratrol's biological properties and its health benefits. From 2005 until the middle of 2010, there have been more than 3,000 new studies on cells, animals, and humans. New and surprising revelations are being announced almost weekly

now by the leading universities, medical schools and research organizations around the world. All of these discoveries add to our knowledge of resveratrol's remarkable range of health and disease prevention effects and gives us new ideas on how to apply this knowledge for the good of mankind.

The reservations expressed by some physicians and science journalists a few years ago about possible side effects, or over estimation of the benefits of resveratrol, have been almost entirely refuted; and new previously unimagined benefits are being revealed as more funding is devoted to animal and human clinical trials of this remarkable natural chemical. At a time when we face multiple drug resistant bacteria, an explosion in the incidence of diabetes, pandemic levels of obesity, debilitating increases in Alzheimer's disease and other forms of dementia, and many other diseases of aging, it is clear that resveratrol is a chemopreventive whose time has come.

No single molecule or drug known to medical science has shown the wide range of potential preventative, therapeutic, and quality of life enhancement properties of resveratrol. It has been shown to inhibit cancer, kill bacteria, viruses and fungal infections, extend life span in animals, improve energy production in cells, quench damaging free radicals, increase glucose tolerance in diabetics, improve cardiac function, enhance physical and mental fitness and concentration, repair damaged DNA, prevent cell damage from nuclear radiation, and much more.

Penicillin has been shown to have one use: to combat bacterial infections. Its effectiveness has been greatly diminished over the past twenty years as many strains of harmful bacteria have acquired resistance to it. Time will tell if resveratrol does fulfill its promise as a so-called miracle molecule, but if it only proves to possess 10 percent of the health and medical benefits researchers have attributed to it so far, it will indeed

make a greater contribution to human health then penicillin, and perhaps even all antibiotics.

Vintage wine versus a lowly weed

Given all of the recent publicity about the health benefits of drinking wine and the so-called French Paradox, one would naturally assume that the principal source of resveratrol used by scientists and supplement makers is the red wine grape. Although the skin of red grapes does contain small amounts of resveratrol, the concentration is much too low to make grapes an economical source of this compound.

Another problem with the extraction of resveratrol from grapes is the difficulty in removing the residues from pesticides, fungicides, and other agricultural chemicals needed to protect the fruit while it ripens. The application of agricultural chemicals not only poses a serious problem from contamination by toxins, but also tends to reduce the natural production of resveratrol and other antioxidants by the grape. The highest concentration of resveratrol is found in organic grapes that are stressed by fungus, unfavorable weather, too little or too much water and a lack of pesticides. These conditions also lower the wine production levels but often result in a wine of outstanding quality.

If the amount of resveratrol in red wine is inadequate to explain the French Paradox then what is the reason the French suffer 40 percent less heart disease than the average westerner? As anyone who has spent time in France knows, the typical French urban diet is high in fats and salt and other less-than-ideal ingredients from a health standpoint. In spite of this fact, the French people tend to have far lower rates of cancer and cardiovascular disease than do Americans. Even lung cancer rates are relatively low amongst the tobacco-loving French

citizens. Furthermore, France has more people over the age of 100 than any other European country. Many scientists now believe that it is the full range of polyphenols, not only resveratrol, which accounts for the chemopreventive effects of drinking wine.

There is another paradox, which is called the American Paradox. The American Paradox refers to the fact that even though Americans are amongst the best fed and most affluent people in the world, their rate of mortality from cancer and heart disease, and more recently, diabetes and the effects of obesity, is extraordinarily high compared to many other developed countries. Wine consumption in the US is relatively low and the typical American and UK diet is heavy on bad fats, red meat raised on antibiotics, growth hormones and other chemicals, high fructose corn syrup, processed foods and chemical laden burgers and other fast foods. These factors, along with too little exercise, too much stress, not enough sound sleep, and a heavy reliance on pharmaceuticals to treat chronic conditions, surely account for much of the serious diseases in the US. They also result in a shorter health span.

Health span is the number of years a person lives free of the so-called diseases of aging. A person who dies at the age of 85 who manages to avoid cancer, diabetes, heart disease and neurological conditions such as Alzheimer's and dementia has a far longer health span than a person who dies at the same age after many years of intensive medical treatment and a dramatically impaired quality of life due to chronic disease and incapacity.

So, if grape skins are not the preferred source of resveratrol, then what is? The answer is the Japanese Giant Knotweed plant, aka Polygonum-cuspidatum. If there were a master ninja of the plant kingdom, it would surely be Japanese Giant Knotweed.

This voracious predator is one of the toughest and most aggressive plants in existence. Above the ground it appears to be much like any other docile flowering green perennial but under the surface its roots tell a different story. If you can imagine a gnarly, hard, dense, thick brown mass that resembles the roots of a mature oak tree, you have a good idea of what the roots of this plant look like. It thrives just as well in high and low altitudes, in hot and cold, and in wet or arid climates. It seems to actually grow stronger in more hostile environments. It is an aggressive invader and, once established in an area, will overwhelm existing vegetation within a few years. It is so tough it has been known to grow up through concrete building foundations.

In Japan and parts of Europe, a fierce battle is waged by farmers and local councils to eliminate or at least control it. In mid-2010, the government of the United Kingdom took the extreme measure of approving the importation of a worm known to thrive on the roots of the Polygonum-cuspidatum plant in a rather desperate attempt to rid England and Wales of the invasive weed. British and Asian farmers who have tried to remove infestations of Japanese Giant Knotweed will tell you that if even one centimeter of the root of one plant is left in the ground the plant will return with a vengeance within a year or two.

This obnoxious plant is the principal source of the resveratrol used in thousands of studies on cells, animals and humans. It is also a 2,000-year-old traditional medicine in China and Tibet.

Resveratrol functions as the immune and defense systems for this plant and many others. Although resveratrol is found in peanuts, blueberries, and many other plants, the concentration of resveratrol is highest in Knotweed. Not only is the plant rich in resveratrol, it is also a source of other natural protective compounds with names like polydatin, pterostilbene, and emodin, which western scientists are only beginning to investigate. Some of these so-called resveratrol analogs appear to be even

more potent than resveratrol in fighting specific diseases and improving health.

Pterostilbene, for example, a compound closely related chemically to resveratrol, has been shown to reverse decline in mental function in rats whose cerebrums were chemically damaged even better than resveratrol or any pharmaceutical. It also has potent cholesterol lowering properties. Many scientists believe that the optimum health and medical effects will follow from combining resveratrol with other chemopreventive plant extracts such as pterostilbene, fruit-based polyphenols, and other phytochemicals. As one physician and researcher recently stated, "Antioxidants are not solo acts, they perform best as players in a diverse symphony orchestra."

Can a molecule that protects plants also protect humans?

In 2006, scientists working at Harvard began referring to resveratrol as a hormetic. A hormetic is a substance that is produced by a plant in response to stresses such as fungus, bacteria, insects, heat, and too much sunlight, which protects the plant against damage or infection. The theory of zenohormesis is that these substances also provide protection and early warning of environmental threats to the animals in their vicinity who consume them, either by eating the whole plant or, in the case of humans, a concentrated form of the plant compounds, such as in a supplement.

Hormetics, such as resveratrol, do not normally act directly on the illness or biological stressor, as do most drugs. They do not function like conventional medicines such as antibiotics, painkillers, cancer drugs, and blood pressure regulators; nor do they generally possess the toxic-

ity of synthetic drugs. These natural plant-derived compounds work by kick-starting processes within the animals' own cells and organs, which attack disease or protect against the stress and harmful environmental factors.

One example of a way in which resveratrol protects animals is its ability to prevent and reduce inflammation by suppressing certain proteins produced by the body in response to infection, injury, and other stresses.

It is now well known that inflammation, rather then simply being a symptom of disease as once thought, is itself the cause of many human afflictions. We have very compelling evidence, for example, that inflammation plays a key role in autoimmune diseases such as arthritis, allergies and multiple sclerosis, as well as many other illnesses including heart disease, diabetes and Alzheimer's disease.

When resveratrol is consumed it does not directly reduce inflammation. Instead, it activates systems in the body's cells and proteins that reduce inflammation naturally. This is why resveratrol is called a regulator or a potentiator, and not a drug. A regulator works by activating or deactivating various enzymes, proteins and even genes to prevent or treat the cause of a problem, not simply mask its symptoms.

When is the last time you heard of a synthetic drug that actually cured any disease? Resveratrol inhibits inflammation by activating many of the same processes that are activated by anti-inflammatory drugs, but in a more sophisticated and precisely targeted manner. Comparing resveratrol with NSAIDS, non-steroidal anti-inflammatory drugs, is analogous to comparing a scalpel to a bread knife. Resveratrol reduces inflammation without also interfering with the beneficial processes that the anti-inflammatory drugs inhibit. It also does not have the unwanted

side effects of drugs such as aspirin, ibuprofen, and the more recently released next generation anti-inflammatory drugs.

The manner in which resveratrol attacks cancer is another example of its selective, almost intelligent effects on cells. Resveratrol inhibits the growth of cancerous cells through a number of different actions. It inhibits the growth of small blood vessels that feed a tumor, but does not stimulate the spread of the tumor to other areas of the body, a process referred to as metastasis, which is one side effect of the anti-cancer drugs, which also inhibit the supply of blood to a cancerous tumor. It also works by activating or deactivating certain proteins such as Tumor Necrosis Factor, TNF, an important immune system molecule that characterizes many tumors, and by suppressing NF-kB, a protein which is linked to almost all cancers in humans.

Many of these anti-cancer effects of resveratrol are the same effects that the pharmaceutical companies are spending billions of dollars to reproduce in new pharmaceuticals. Unfortunately, many of the more effective drugs being used today are also highly poisonous to the patient as well as to the tumor. Often it is a death race for the patient between the drugs' toxic effects and the growth and spread of the cancer.

One oncologist I spoke to at M.D, Anderson Hospital in Houston said; "Very few people are actually dying of cancer these days. With aggressive treatments such as chemo, radiation and surgery most die of the therapy first, or if they are lucky they survive both the cancer and the treatment."

This is not to propose the use of resveratrol as a treatment for cancer, or any other disease for that matter. We need much more actual human clinical data and confirmation of the results seen in the 4000 plus studies, trials and investigations already completed before we can say with confidence that resveratrol is as effective as the laboratory studies

indicate it should be against any specific disease. It may well turn out that some combination of resveratrol and the more effective anti-cancer drugs will be the best strategy to pursue. We know for example that, in the case of some chemotherapy agents, resveratrol improves their effectiveness and reduces the severity of their side effects. It may also turn out that some other phytochemical, such as Pterostilbene, may be even more effective than resveratrol. There is presently an enormous amount of research being undertaken to answer these questions.

Why smaller is better

The larger and more complex a molecule is, the harder it is for the molecule, be it a drug or nutrient, to be taken up by the cell. It's also very often less effective against the basic process or disease being targeted. Larger molecules are also more likely to have unpredictable side effects.

Smaller molecules are better able to pass through the cell membranes, which act as barriers surrounding all cells. They are also better able to precisely target individual disease components at the cellular level. The effects of large molecules, which constitute most pharmaceutical drugs on the market today, versus small molecules, such as resveratrol, is the difference between using a laser to remove a tumor versus removing the entire organ or limb surgically.

The major drug companies, such as Biotica and Genentech, as well as research organizations, including the National Institutes of Health, consider small molecule drug candidates to have the greatest potential as treatments for diseases such as arthritis, Alzheimer's disease, cancer. In the areas of gene therapy, and neurological diseases such as Alzheimer's disease, larger molecules are essentially ineffective due to their inabil-

ity to pass through the blood brain barrier, the protective barrier which prevents potentially damaging chemicals from entering the brain. Only small molecules can pass through this protective filter.

Resveratrol is an exceptionally small molecule that has shown astonishing effects in thousands of animal and laboratory studies. In the past few years, many of the health and longevity effects seen in the laboratory have also been confirmed in human clinical trials. We now know in much finer detail how resveratrol operates at the cellular level to affect the body's systems and functions. Going forward, the emphasis of researchers will shift from cell and animal trials to clinical trials on humans. Results from these limited human studies so far have been nothing short of astonishing. It is expected that progress in discovering new medical and health enhancement applications for resveratrol over the coming decade will be rapid and dramatic.

Resveratrol and aging, life span versus health span

Increases in the maximum and average life span of humans from the beginning of the twentieth century until now have not been particularly impressive compared to the advances made in other areas of science and technology; and in some countries, such as Russia, life spans have actually declined. Predictions by demographers of a drop in the average US life span in this century are based upon compelling evidence of declining health amongst the present generation of teens and twenty-somethings, made worse by the rising cost of health care.

Our poor record in extending maximum life span is attributable to the fact that medical technologies and pharmaceutical research have focused more on keeping sick people alive rather than on preventing

the diseases and disabilities related to aging. Drug companies make far more money selling drugs that treat disease than on cures to diseases. This is one reason why virtually no cures have been offered by any major pharmaceutical company in the last 25 years.

One result of corporate greed-driven medicine has been that the average person spends more than 90 percent of his or her lifetime medical expenditures during the last five years of life. Although average life spans have increased moderately over the past two decades, health span, the number of years one enjoys a healthy, independent, and productive life, has not kept pace. In fact, health span appears to be decreasing in the US, the UK and in much of Asia, as the citizens of these countries forsake traditional diet and remedies for the western lifestyle.

One rather alarming prediction is that parents now aged 45 to 60 may commonly outlive their children for the first time in history. At the current rate of increase of medical costs, the policy of treating disease rather then preventing disease is unsustainable. At some point during the next ten to twenty years the result will be that health care, and consequently life span, will be severely rationed, or national budgets for health care will consume more than the total government revenues for all public services. Preventable diseases such as type 2 diabetes, many cancers, and cardiovascular diseases are increasing in incidence at unprecedented rates in the developed world. Many physicians and scientists believe that resveratrol can play a critical strategic role in reducing run away health care costs by preventing, delaying or treating many of the health conditions associated with poor diet, lack of exercise, and obesity.

Most of what you think you know about aging is wrong

This applies whether you are a laymen, physician, political leader, science journalist, social scientist or author of books and articles on the subject. To begin the process of dismantling the prevailing myths and misconceptions here are a few facts to consider.

"Aging and the widely recognized diseases of aging are the inevitable consequences of living longer."

FALSE: Aging is not in itself the cause of diabetes, obesity, heart disease, cancer or Alzheimer's. Nor does aging necessarily lead to impairment of emotional health, physical capacity, libido, cognition, memory or intelligence. Aging is merely the name given to the constellation of adverse health and medical conditions normally associated with the elapse of time since one is born. The diseases and disabilities associated with advancing age all have specific causes. One's age is simply a measurement of time lived, and time is not in itself a cause of any disease. By modifying one's diet and daily routine, staying physically and mentally active, adopting preventative lifestyle practices, and seeking appropriate medical interventions to repair, replace and renovate deteriorated body parts and capabilities, virtually all of the diseases normally associated with chronological aging can be either delayed, prevented or even reversed.

Adopting preventative strategies at the individual level can radically lower the mortality rate from disease, and one such strategy is the intelligent use of supplements such as resveratrol. Unfortunately, the institutionalized profit motive driving the emphasis on treatment versus

prevention deprives the majority of the world's population of the benefits of increased longevity and improved health during later life. Only those individuals who take personal responsibility for their health can expect to achieve improved health and life spans.

"An aging population will be a drag on society, the young, and the economy."

FALSE: Precisely the opposite scenario to this almost universally predicted calamity will actually ensue.

The science commentators and social scientists who contend that an increased population of older citizens will be a burden on the younger members of society fail to understand one very simple fact; many people will live longer because they are free of the disabling medical conditions which presently drain the wealth, vitality, and productivity from society.

It is foolish to presume that people will somehow magically live substantially longer without concurrent improvements in their health and vitality. An elderly professional man or woman, for example, who is still healthy, energetic, and mentally sharp is greatly advantaged over a younger colleague by virtue of his or her additional years of work experience, judgment, and maturity.

Think about it. Given the choice between two surgeons, both of whom are fit and healthy, would you prefer the doctor with 40 years of experience and thousands of operations under his belt to remove your ruptured appendix or the surgeon with five years and only 100 operations?

Industry and the professions are already seeing a surge in demand for older workers over their less experienced colleagues in all developed

countries. As average health span increases we will see people taking up new careers and starting university at the age of 50 and greater, professional athletes in their 40s and 50s will challenge competitors who are decades younger, and the average retirement age will increase dramatically, which means that many more people will be paying taxes and contributing to the economy for five to twenty years longer during their life times. Importantly, many fewer people will be drawing retirement and disability payments or requiring costly medical treatments.

If prevention and personal responsibility for health become a reality, the improvements in health span could be the single largest contributor to the US and UK economies twenty years from now. Resveratrol and other natural compounds related to resveratrol may have the potential to add many productive years to the life of westerners by extending health span and inhibiting conditions such as dementia, diabetes, cardiovascular disease and cancer.

"There is an intrinsic biological limit to the number of years humans can live healthy, vital, independent lives."

FALSE: Scientists have yet to identify a ticking "biological clock" that predetermines the maximum life span for a human. Humans are not "programmed" to die at a certain age. We know what the principal causes of aging are, and we are rapidly closing in on solutions to these causes. Some, such as the corruption of one's DNA, and decreasing telomere length, which occurs as cells divide, are a bit more complex than others, but none are impossible to solve given the application of sufficient resources.

A Manhattan Project style attack on aging would probably solve all of these challenges in fewer than ten years. Now that the medical and research communities are beginning to treat aging as any other disease,

rather then accepting it as inevitable, and simply focusing on making older people more comfortable, we can expect dramatic breakthroughs in life extension. Each new breakthrough will give humans a bit more time during which new discoveries will be made that will create stepping stones to the final goal of indefinite life span.

Resveratrol is known to be a chemoprotective agent, which can play a critical role in delaying or possibly even preventing the most serious causes of mortality in the developed world. Serious consideration should be given to incorporating resveratrol and other natural chemopreventive supplements into a more rational, humane and effective national health plan in every developed country. Unless the priority shifts from treatment to prevention, the health, wealth and life span of citizens will continue to decline and national health care budgets will be unable to keep pace.

"A silver bullet is just over the horizon that will dramatically extend human life span."

FALSE: The increase in human longevity will come in small steps which will turn aging from a debilitating terminal disease into a treatable condition just as the case has been with diseases such as diabetes, HIV-AIDS, malaria, and many others.

Resveratrol is not a magic elixir that will prevent the diseases of aging or compensate for poor health habits. Like stem cell therapy, genetic engineering, organ replacement, natural and synthetic drugs, exercise, diet and medical technology, it has an important part to play in any longevity program. As we collect more data from human clinical trials we will be better able to define just what this role should be.

Resveratrol is only the first in what will likely be a long list of similar compounds with extensive health benefits. Other compounds related to resveratrol, such as Pterostilbene, Polydatin, and various other analogs of resveratrol, will be intensively investigated over the coming few years, and it is almost certain that researchers will find a treasure trove of genetic and other biological effects even more impressive than those of resveratrol.

Pterostilbene, a natural compound found in blueberries, for example, has been shown in rats to actually reverse declines in decision-making abilities and appears to improve intelligence. It also lowers LDL cholesterol more effectively than resveratrol does. Polydatin is more effective than resveratrol in preventing the damage to heart tissue occurring when a heart attack victim is resuscitated or a heart is restarted following some types of cardiac surgery. Emodin, an antioxidant found in the Japanese Giant Knotweed plant, is a potent anti-cancer agent.

The more we learn about these astonishing molecules, the more we are awed by their benefits to human health. Many researchers have noted a synergistic effect when resveratrol is combined with other polyphenols such as curcumin, however not all combinations of polyphenols are synergistic. For example, a negative effect on Sirt gene activation has been observed when resveratrol is combined with the antioxidant quercetin.

Health span and life span will increase as discoveries are made and knowledge is created that will lead to cures and therapies to treat the so-called diseases of aging. Natural chemoprotectives such as resveratrol, curcumin and a wide range of other polyphenols may take over much of the role synthetic drugs now play in treating disease after the fact rather than focusing on preventing disease naturally.

"Technology advances will lead to longer life spans and elimination of many diseases."

TRUE: Dr. Sinclair at Harvard University discovered the gene activation properties of resveratrol only because he had the help of a new computerized chemical screening system that could examine thousands of molecules for their anti-aging gene activation properties in the time it previously took to investigate only a handful of compounds.

Advances in computing power are rapidly increasing our ability to comprehend the intricacies of the metabolic process and to realistically simulate critical biological pathways. The past decade saw the development of genomics. The coming ten years will consolidate this knowledge and move on to unraveling the role of the proteins which are encoded by our genes. This will represent an enormous advance in our ability to design drugs that turn on beneficial genes and switch off the genes responsible for diseases such as multiple sclerosis, asthma, cystic fibrosis, thalassemia, mental illness and hundreds of other diseases that are caused by either a specific genetic abnormality or a combination of genetic factors.

We will also begin to solve the mystery of what function the 95 percent of the genome which does not code for proteins plays in human development. This will lead to the design of new strategies to prevent or reverse aging and result in quantum leaps in human longevity. By 2020 computers and other medical devices will be powerful and cheap enough to give scientists the tools they have needed to virtually stop the aging process in animals. This goal has already been achieved in the lab.

The convergence of thousands of independent discoveries and incremental breakthroughs by dedicated professionals working in diverse

fields are creating synergies and mutually reinforcing discoveries that are the key to extending life span and eventually eliminating aging altogether. Developments in advanced prosthetics, stem cell therapy, organ replacement, and the prevention and treatment of cancer, heart disease, and neurological conditions such as Alzheimer's and dementia will mean that those persons who are presently under 60 years of age and in excellent health will have a reasonably good chance of living indefinitely. This assumes that they are financially able to afford the treatments, drugs, and therapeutic procedures, which will become available over the next 30 years.

Beyond 2040, aging will be simply a chronic condition treatable or preventable at a reasonable cost to the patient. The timing of one's death will become for many people a matter of individual choice. Accidents and needless wars over resources will become the main causes of death in the developed world. Unless we stop destroying our planet through the plundering of its resources and poisoning its air and water, climate change and scarcity of usable water and breathable air will render any increases we make in average life spans a waste of time and effort. If we destroy the vital balance, which sustains life on this planet, nothing else will matter.

"We must first fully understand the cell's incredibly complex metabolic process before we can develop effective drugs and other preventatives and treatments for the disease we call aging."

FALSE: Many of the safest and most successful drugs in use today work by targeting unidentified biological processes they were not initially designed to attack. Luck plays a big part in drug discovery. Serendipity and persistence on the part of researchers and physicians resulted in the discovery of penicillin, aspirin, pain killers

and many other valuable drugs. Partial knowledge of the cellular-level biological processes being targeted, coupled with the intelligent application of trial and error, is an effective and rational life extension strategy. It probably offers the greatest potential to conquer aging in the near- to mid-term.

When Dr. Sinclair discovered the ability of resveratrol to activate the so-called anti-aging genes, it was due to serendipity as much as to science. Sinclair discovered this previously unknown ability of resveratrol because he was able to quickly screen thousands of chemicals for this property due to advances which had just been made in laboratory analysis technology. His discovery did not come about because he had some reason to believe that resveratrol might fit any receptor on a cell or it might have anti-inflammatory or antioxidant properties. In fact, so called rational drug development, in which computers attempt to match chemicals to cell receptors in a search for drug candidates, has failed to live up to its promise.

Why are we aging faster but living longer?

The decline in the health status of the average British or American citizen is not principally a natural or inevitable consequence of human evolution nor is it due to the rise of new diseases or the deterioration of the quality of the environment in which we live, although environmental factors do militate against increasing life spans. The fundamental causes are simple and well known.

Life span increases so far have come about only because advances in medical technology and pharmaceuticals are keeping sick people alive longer, but at a very high and untenable cost, not because dis-

eases and disabilities are being prevented or that people are staying healthy longer. Further increases in both health span and life span must come from adopting prevention as our primary focus. We have yet to begin to exploit the advantages of prevention at the institutional level. Resveratrol is one molecule that may play an important part in both prevention and treatment of disease.

Obesity and life style factors, not aging, are the principal cause of diabetes, hypertension, most heart conditions, and most cancers. Obesity is also a major causal factor for gastric reflux disease, gall bladder disease, degeneration of L-sacral spine and weight-bearing joints, asthma and hundreds of other adverse medical conditions. Resveratrol was shown to increase the life span and health span in obese mammals. In Dr. Sinclair's now famous study published in the journal Nature, obese rats fed resveratrol lived 31 percent longer. When the vital organs of the resveratrol-fed rats were examined by a pathologist they resembled those of young, lean, healthy rats.

Lack of regular exercise compounds the negative medical consequences of obesity, and is a risk factor for osteoporosis as well as a wide range of adverse physical, emotional and neurological conditions. Mitochondria are the cells' energy factory. Resveratrol increases mitochondrial density and enhances mitochondrial function. Rats fed resveratrol in the study by Dr. Auer and published in the journal Cell, were able to run twice as far as rats not fed resveratrol. When the muscle tissue of resveratrol-fed animals is examined under a microscope, the increased number and health of the mitochondria is evident.

Probably the largest contributor to early aging and the diseases associated with aging is poor diet. Excessive consumption of red meat, processed foods, sugars and high fructose corn syrup, as well as trans fats and the lack of omega-3 rich foods and polyphenols from fruits and green leafy vegetables, and overeating in general are all enemies

of human health span and longevity. Resveratrol has been shown to counter many of the adverse effects of poor diet. We know that obese rats fed resveratrol in Dr. Sinclair's study outlived the rats not fed resveratrol, but it is less well known that the resveratrol-fed rats also avoided all of the normal diseases associated with aging and obesity.

Chronic unresolved stress results in endocrine imbalances, immune system dysfunction, inflammation, sleep disorders and neurological impairment. Resveratrol is a natural anti-inflammatory agent and may have important neuroprotective properties. In a study done at Northumbria University in the UK, students who were given either one or two Bioforte capsules containing 250 mg of trans-resveratrol experienced a 100 percent to over 200 percent increase in brain blood flow.

A prescription for longevity

Anyone can substantially increase both health span and life span by adopting the following measures:

- Stop using tobacco products of all types and limit alcohol use to no more than three glasses of wine or three ounces of spirits per day.

- Reduce, or better yet eliminate, all processed foods, fast foods, and sweetened beverages. Make green leafy vegetables your primary food group. Reduce or eliminate red meat from your diet.

- Take a pill. Add the below supplements to your daily routine:

- Biotivia or other quality resveratrol, 250mg to 1,000mg

- Pterostilbene, a molecule closely related to resveratrol, 100mg daily.

- Non-fish sourced omega-3, such as Green Omega 3, with EPA and DHA, at least 500mg.

- A multi-antioxidant (not multivitamin) complex such as Bio Quench, 500mg to 1,000mg

- Vitamin D, 10,000 IU. Most people are deficient in this important nutrient.

- Acetyl L-Carnitine and Alpha Lipoic Acid supplements, 250 mg of each.

- Curcumin, also known as the spice turmeric, 1 to 2 grams per day.

- Vitamin C, preferably the oil soluble form called ascorbyl palmitate, 1 gram per day.

There are, of course, many other supplements that may have a beneficial impact on health span and longevity, but the published scientific evidence best supports the above nutrients. The majority of over-the-counter supplements are of very little chemoprotective value.

In addition to the above supplement regime, incorporate the following into your daily routine:

- Incorporate at least 30 minutes of moderate to intense exercise, at least three times each week, into your routine. Get up from your computer, video games, iPad, email, and Facebook accounts and do something physical, preferably outdoors. Even if you are overweight

you can be fit. In fact, it is healthier to be fit and fat then unfit and thin.

- Meditate, or at least take a one-hour mental and physical break from your daily grind, once each day. Midday naps of 20 to 45 minutes are also extremely beneficial.

- Maintain a healthy weight, which is best measured by dividing your height in inches by your waist circumference. The result should be no less than 2.0. The popular BMI measurement is basically worthless, as it makes no distinction between lean and fat body mass.

- Use high quality air and water purifiers in your home and office. Lobby your political leaders to take environmental protection and clean energy seriously. At some point the limit on life span will be the determined by the ability of the Earth's climate and resources to support human life.

- See your physician at least once per year and repair failing parts just as you do with your automobile or any other complex machine. If your eyesight is deteriorating, consider having a corrective procedure by an eye surgeon, If you have dental or periodontal issues, see your dentist and get them sorted before they lead to serious disease. Teeth and gum infections can cause fatal heart disease and other life threatening conditions.

- Do not ignore symptoms of an underlying problem. Your chances of surviving cancer, as we all know, are dramatically enhanced if you begin treatment early. The same rule applies to diabetes and most other chronic diseases.

- Drive sensibly, wear seat belts and control your stress. It would be a pity to live a healthy life and then die at the age of 40 on the motorway.

- Use an advanced UV protection product to control photo aging of the skin. Resveratrol has been shown to both prevent and reverse the DNA damage, which ages the skin. One cream that contains resveratrol in high concentration along with other polyphenols is Celle by Biotivia.

What the science says

The most recent research results by scientists and physicians working at prestigious medical schools and other institutions around the world were presented in September of this year at the Resveratrol 2010, the first international science conference on resveratrol and health. There is not enough space in this paper to discuss all of the remarkable results presented by the experts at this conference. I have chosen to summarize the high points of some of the more interesting and authoritative studies below. It should be noted that no study was presented in which any toxic or serious adverse effect of oral administration of resveratrol to animals or humans was observed, and no study or trial was stopped due to the presence of such negative effects.

Resveratrol human clinical trials

Over the past three years a substantial number of medical schools and research institutions have undertaken studies of resveratrol's ability to prevent or treat disease in humans. The number of such clinical

trials is increasing weekly. A few of the more important ones are described below.

Diabetes

Albert Einstein Medical College conducted two human clinical trials in which the ability of resveratrol to enhance mitochondrial function and improve insulin sensitivity, two important functions the drug companies are attempting to target with a new generation of diabetes drugs.

The results of this study were extremely positive and it was recently announced that this small-scale study using Bioforte resveratrol will be expanded later this year by Albert Einstein Medical College in collaboration with the Mayo Clinic. Although there are several other human clinical trials either underway or about to commence, the Einstein/Mayo Clinic study is the one to look out for. The results of this relatively large-scale double-blind trial will likely answer the question of resveratrol's potential usefulness as an alternative to some of the present side effect laden pharmaceuticals.

One such new generation diabetes drug announced at the annual science conference of the American Diabetes Association in Orlando Florida warned that two adverse effects had been seen in the FDA mandated drug trials of this compound. The first was that the drug can actually cause someone who does not suffer from Type 2 Diabetes to contract the disease, and the second was that it had the nasty tendency to lower blood glucose levels so severely that the patient could die. Other diabetes drugs have been taken off the market after life-threatening side effects were discovered.

Heart Disease

Stony Brook University Medical Center, a renowned cardiac center in New York, has begun a long-term human study of resveratrol's potential ability to prevent patients who have suffered one heart attack from having a second one, or increasing the chances that, if the patient does have a subsequent infarct, he or she will survive it.

The ability of resveratrol and pterostilbene and polydatin, analogs of resveratrol, to prevent the cardiac tissue damage that occurs when a heart, which stopped beating due to a heart attack or open heart surgery, is perfused with oxygen. Interestingly enough, the tissue damage,, which heart attack victims suffer, does not happen while the heart is stopped, even for considerable lengths of time. The damage occurs due to a flood of destructive free radicals, which occurs when oxygen again flows through the tissue. This finding suggests that paramedics might one day be equipped with injectable resveratrol to administer to patients whose hearts have stopped prior to perfusing the heart with oxygen.

COPD, Chronic Obstructive Pulmonary Disease

COPD is a common but serious and debilitating condition caused by inflammation of the tissues of the lung and the resulting inability to deliver sufficient amounts of oxygen to the blood and to remove accumulated carbon dioxide. Sufferers of this condition constantly feel that they are suffocating. COPD affects millions of people and is a common disease of smokers and people who have worked for many years in a highly polluted environment, such as a chemical factory or mine. Imperial College of London has obtained an international patent on the use of resveratrol to treat COPD. As of this publication no medicine has been developed by any pharmaceutical company on the basis of this patent, however the University of Torino, founded in 1404 and the home of two

recent Nobel Prize winners, is about to embark on a study of smokers to study resveratrol's ability to alleviate the pulmonary inflammation caused by their habit.

Metabolic syndrome, pre diabetes and non-alcoholic fatty liver disease

A study funded by the Danish government is about to begin in June 2011. The lead researcher is Dr.Steen Bønløkke Pedersen from Aarhus University. The project will include a one year randomized double-blinded study of 50 subjects. Aside from Aarhus University and Fluxome, the Aarhus University Hospital, University of Southern Denmark, Roskilde University and Pennsylvania State University will contribute to the clinical trial. This $3.5 million human clinical trial will investigate resveratrol's potential to treat and prevent a constellation of human health conditions which are known to accompany aging. This will be the most extensive and best-funded long-term human clinical trial to date. The knowledge gleaned from this investigation will be invaluable in assessing the potential of resveratrol to alleviate a range of adverse health consequences which afflict millions of people worldwide.

"We expect to prove that resveratrol in humans can neutralize the detrimental effect of obesity on whole body metabolism, like low-grade chronic inflammation, insulin resistance and lipid infiltration in liver and skeletal muscle," Dr. Pedersen said.

Thalassemia

Beta Thalassemia is an inherited disorder in which either very few or no red blood cells are produced by the bone marrow after infancy. The treatment is monthly whole blood transfusions and the use of a drug

which is extremely toxic and cannot be used with children. The disease dramatically impacts the sufferers' quality of life and often results in death around the age of puberty. Because it is more common in less developed countries where it is virtually impossible for anyone other than the very wealthy to obtain regular supplies of clean whole blood for the required transfusions, the fatality rate is high. Even if the patient is able to obtain monthly transfusions and is able to afford the drugs to treat the disease, he or she is constantly anemic and lacking of energy.

Dr. Roberto Gambari, physician and molecular biologist, and well-known authority on Beta Thalassemia, at the University of Ferrara, discovered that Transmax resveratrol, the concentrated pure resveratrol supplement used by researchers in most clinical trials, was able to stimulate the production of embryonic red blood cells, the type that are produced when a baby is still in the mother's womb, but soon after birth cease being produced. This is an extremely important finding and one that has led to a human clinical trial now underway at the University of Ferrara. The subjects in this clinical trial are hospitalized, adolescent Beta Thalassemia patients. Hopefully resveratrol will give a new lease on life to those who suffer a disease that the pharmaceutical companies do not consider potentially profitable enough to develop a new drug for.

Brain blood flow and cognition

In 2010 Northumbria University, located in northeastern England, conducted a human clinical trial in which university students were given either one or two Bioforte capsules, each containing 250mg of trans-resveratrol. The objective of this study was to assess the effects of oral resveratrol on cognitive performance and localized cerebral blood flow variables in healthy human adults.

In this randomized, double-blind, placebo-controlled, crossover study, 22 healthy adults received placebo and 2 doses (250 and 500 mg) of trans-resveratrol in counterbalanced order on separate days. After a 45-minute resting absorption period, the participants performed a selection of cognitive tasks that activate the frontal cortex for an additional 36 minutes. Cerebral blood flow and hemodynamics, as indexed by concentration changes in oxygenated and deoxygenated hemoglobin, were assessed in the frontal cortex throughout the post treatment period with the use of near-infrared spectroscopy. The presence of resveratrol and its conjugates in plasma was confirmed by HPLC after the same doses in a separate cohort (n = 9).

Resveratrol administration resulted in dose-dependent increases in cerebral blood flow during task performance, as indexed by total concentrations of hemoglobin. There was also an increase in deoxyhemoglobin after both doses of resveratrol, which suggested enhanced oxygen extraction that became apparent toward the end of the 45-minute absorption phase and was sustained throughout task performance. Cognitive function was not affected. Resveratrol metabolites were present in plasma throughout the cognitive task period. The second phase of this trial is currently underway. In this human clinical study the students will be given daily doses of Bioforte resveratrol over a period of one month versus the single dose regimen of the first trial. Additional parameters, such as resveratrol's effect on the students' weight, sleep patterns and mood will be examined in this trial.

Fitness and physical performance

The University of Texas is conducting a human trial to investigate resveratrol's effect on human athletic performance and physical endurance. The trial, also using Transmax, is presently underway and results are expected in about two months. Dave Noble, a 64-year-old American who

participated in competitive swimming events as a twenty something, started to compete again after a 40-year sabbatical from the sport. Dave began using a resveratrol supplement, the same one used in most of the medical school trials, after six months of training. Within two months of beginning supplementation with resveratrol Dave was breaking personal records that he set when he was in his early twenties. As of 1 May 2011 Dave was within the top five amateur swimmers worldwide for his event and category. Dave credits resveratrol for his athletic improvement. He takes 500 mg of resveratrol about 45 minutes prior to training and competing, and credits the compound for his success. He has been competing now for about three years since starting again at the age of 61, and each month his times improve and his endurance, as measured by maximum oxygen uptake, known as VO2 Max, is increased.

A guide to selecting a quality resveratrol supplement

Since the study by Dr. David Sinclair was published in the journal Nature, a plethora of new companies have sprung into existence offering resveratrol supplements. Evaluating resveratrol sellers and their products has become a confusing and frustrating process. This guide is meant to elucidate the most important factors one should use to distinguish one resveratrol supplement from another based upon their relative quality, value and likelihood of being effective.

Unlike most dietary supplements, thousands of well managed authoritative scientific studies and trials have highlighted resveratrol's potentially critical health properties as a treatment for diabetes, cancer, inflammatory and autoimmune diseases and neurological conditions. Without passing judgment on resveratrol's actual curative powers, it is clear that many people purchase resveratrol as a preventative or treat-

ment for a serious medical condition. If the resveratrol these consumers purchase is not a high quality, properly manufactured, bio active compound then they are not only wasting their money but are also failing to obtain whatever benefits resveratrol may offer for the prevention or treatment of disease.

The criteria below are based upon valid scientific principals and accepted standards for the evaluation of a functional dietary supplement such as resveratrol. The standards can also be used in judging other supplements.

Your supplier

After the Dr. Sinclair study was published in the journal Nature, a flood of new, inexperienced and ill equipped online resveratrol suppliers suddenly started to promote this compound. Many of these companies and individuals engaged in unethical and deceptive marketing campaigns, which lured customers in with phoney “free offers” and other inducements. Their products often did not contain measurable amounts of resveratrol and, in many cases, the operators and owners of these companies had a history of fraud. The lesson here is that one is well advised to select a company with a history of at least ten years in the industry, and one which specializes in advanced nutraceuticals, versus a generic supplement maker. Resveratrol is a difficult compound to process and, unless special care is taken throughout the manufacturing process, can easily degrade into a worthless powder.

Ethical labeling

The labels of many resveratrol suppliers do not disclose the exact form of resveratrol or the quantity contained in their supplement. Some simply call their main ingredient "red wine complex" or a "proprietary blend." Given that red wine contains less than 1 percent resveratrol, it seems a bit strange that a company would use this description to label a resveratrol product unless the purpose was to conceal the actual ingredients in the product. A proprietary blend can be almost anything, but is unlikely to consist of pure resveratrol given the relatively high cost of quality resveratrol versus other possible ingredients.

Resveratrol is composed of two principal isomers: trans-resveratrol and cis-resveratrol. Only the trans-isomer has been associated with health benefits. The cis isomer actually acts to nullify the effects of trans-resveratrol. Unless the seller states on the label that the product consists entirely of the trans-resveratrol form it is highly likely that it contains either some or all of cis-resveratrol, which is, by an order of magnitude, the less costly form of resveratrol.

Dosage

The appropriate dosage of trans-resveratrol is a highly contentious issue, with respect to the rhetoric of resveratrol suppliers, that is. The science regarding dosage is relatively clear however. Although doses of around 50 mg to 100 mg appear from some studies to have potentially important preventative effects, the consensus is that at least 250mg is required to reach the threshold for efficacy as demonstrated in most animal and in vitro studies undertaken to date. This equates to the human equivalent of the dosage used in the Dr. Sinclair study and many other studies. The dose recommended by most clinicians for treatment of an existing condition ranges from 1,000 mg to 4,000 mg. However it

is recommended that one consult a physician before taking a dose over 1,000 mg daily. No toxicity or serious adverse effects were observed in several animal and human studies in which up to 5,000 mg was given on a daily basis for an extended period of time. In animal studies, dosages up to the human equivalent of 30,000mg have been tolerated with only minor adverse effects. Products which offer less than 250mg of pure trans-resveratrol are of dubious value.

Source of resveratrol

Although much of the news about resveratrol mentions the red wine grape as its source, wine grapes are not a practical or desirable source of resveratrol for two important reasons. First grapes are subjected to a wide range of toxic chemicals in the cultivation process. Fungicides, pesticides, chemical fertilizers and many more chemicals are sprayed directly on wine grapes. Since resveratrol comes from the skins, it is very difficult to eliminate contamination in the resveratrol concentrate. The second reason wine grapes are not a good source of resveratrol is that it is impossible to produce a high potency supplement using grape extract. The concentration of resveratrol in grape skins is simply too low. This is why, in virtually all of the animal and tissue studies on the health benefits of resveratrol, the source of the resveratrol was the Japanese Giant Knotweed plant, which grows without fertilizers or agricultural chemicals in the wild.

Natural versus synthetic

Synthetic resveratrol can be produced using one of two methods, fermentation and chemical engineering. In the case of fermentation, a yeast or bacteria is genetically modified to produce resveratrol. Chemically engineered resveratrol is constructed from a broth of compounds using

organic chemistry to engineer the molecule. Both processes are fraught with potential pitfalls.

In the case of fermentation often what may occur is that bits of the bacteria or yeast DNA used to produce the resveratrol show up in the finished material. This means that if you use this product, you are consuming a novel substance—a compound that has never been previously consumed by a human, with potentially toxic or other other unknown effects. In the case of a chemically engineered resveratrol product, the issue is contamination by small amounts of the chemicals used to produce the synthetic resveratrol.

On a typical HPLC graph of a synthetic resveratrol there will almost always be spikes on the chart of what are referred to as "unknowns." These trace chemicals are by-products of the creation of the resveratrol which are unidentified and assumed, or hoped, to be non-toxic. Furthermore, naturally extracted resveratrol from the polygonum cuspidatum plant is known to be effective and non-toxic. Neither properties have been definitively verified in regard to synthetic resveratrol. When a natural compound such as resveratrol is copied using chemicals, yeast or bacteria often the final product is not truly identical to the natural compound. There is only one reason why some suppliers use synthetic resveratrol in place of natural resveratrol from polygonum cuspidatum. The reason is the far lower cost of synthetic resveratrol. If a supplier does not disclose which type of resveratrol is contained in its products you can normally assume that it is the synthetic variety.

Capsule size

A size zero capsule is able to contain about 500 mg of resveratrol, but only if the base material is processed using pharmaceutical technology and equipment. This is the largest size capsule that is quite easily swal-

lowed by most people. Sellers who use larger capsules do so to compensate for the fact that they are simply stuffing lower potency raw material into a capsule without going through the time and expense of purifying and granulating the resveratrol extract. A larger capsule size also allows for the use of various fillers and chemicals such as silicon, magnesium sterate, cellulose and other additives. The best quality resveratrol supplements are contained in a size zero, all-vegetable capsule and contain no additives or fillers at all. There is no reason why you should have to consume sand, chemicals, and other unwanted ingredients in your supplement simply because your supplier can not be bothered with using more sophisticated processing and filling technology.

Resveratrol is highly susceptible to deterioration by oxidation and exposure to ultraviolet light

A quality supplement will be protected from oxidation during manufacture through the use of nitrogen gas-filled processing lines. The bottle in which the supplement is contained should also use an inert gas to prevent oxidation during shipment. However once the bottle is opened oxygen is allowed to enter. If active packaging technology is not employed to protect against this damage, the shelf life of the product will be seriously degraded. Many resveratrol supplements are already oxidized when purchased. Only one company uses an active packaging oxygen absorber system to capture the oxygen which enters the bottle when a capsule is retrieved.

Capsules and packaging

The capsules themselves should be made from high quality, all-vegetable materials such as Pfizer Vcaps. Cheaper clear gelatin capsules, which are made from animal by-products, have no place in a resveratrol

supplement. Not only is an all-vegetable capsule healthier to consume than a gelatin capsule, but it is designed to better regulate the release of the active ingredients into your digestive tract. What is the use of taking a high quality natural supplement if the capsule it is contained in is made from the collagen inside animals' skin and bones?

Gimmicks to watch our for

Micronized or nano resveratrol

There is absolutely no published scientific evidence that shows micronization improves the bioavailability of resveratrol. In fact, it may have a negative effect by reducing the half-life of resveratrol in blood plasma. There is no reason to pay extra for a micronized resveratrol product, which offers no practical advantage to the user, and may not be as effective as a good quality granulated resveratrol.

Resveratrol with quercetin

Quercetin is a potent antioxidant in its own right, however it should not be combined with resveratrol or even taken within at least eight hours of taking a resveratrol supplement. The reason, which was only recently discovered, is that quercetin blocks the metabolites of resveratrol from entering your blood stream. Quercetin also deactivates sirtuins, precisely the opposite effect of resveratrol.

Until a few years ago it was assumed that adding quercetin was a good thing since the importance of the metabolites was not understood. Before the latest studies revealed otherwise it was assumed that the metabolites were not responsible for the biological and longevity gene

activation effects of resveratrol. Based upon several highly regarded studies, we now know that it is very likely that the beneficial effects of resveratrol actually derive mainly from these metabolites rather than from the free resveratrol.

These metabolites are bioactive products of the breakdown of resveratrol by the liver and layer of cells lining the small intestine. By blocking these sulphates and glucordinates, quercetin interferes with the ability of resveratrol to activate the sirtuins, specifically Sirt-1 and 2, the so called anti-aging genes, and blocks other signaling pathways through which resveratrol operates, and which are responsible for many of the desirable health effects of resveratrol. Moreover, the half-life of the metabolites in human tissue is several hours whereas the half-life of free resveratrol is only about 12 minutes.

In a 2009 study of resveratrol's effects on inducing the creation of hemoglobin cells in patients' blood it was found that quercetin totally blocked the ability of resveratrol to create the new red blood cells. Quercetin also nullified the anti-inflammatory property of resveratrol in an informal trial of resveratrol's palliative effect on arthritis. There is no scientific justification for adding quercetin to a resveratrol supplement. If one wishes to take quercetin it is readily available as a low cost supplement that may be taken by itself.

Red wine complex

Some supplement makers attempt to confuse the buyer into thinking that he is buying a resveratrol product by using this misleading description. There is no standard for "Red Wine Complex." Red wine contains only very small amounts of resveratrol, less than 5 percent as a rule. Companies who do not disclose the amount of trans-resveratrol in their products should be avoided.

Dr. Oz or Oprah recommended resveratrol

Neither Dr. Oz nor Oprah recommend any brand of resveratrol. If you are interested in knowing which brand they use in their presentations on resveratrol you can find this by searching for resveratrol on their respective websites. The lawyers for both of these respected personalities have taken aggressive legal action against the companies and individuals who claim that they recommend their products.

Five essential criterion to pick a resveratrol provider

Credentials

The media coverage of the studies demonstrating the potential benefits of resveratrol has attracted a flood of new and clearly disreputable resveratrol sellers to the market. These companies have no experience in producing a food or health supplement, no scientific staffs, testing labs, or other technical resources. Most have no established quality control standards and no history by which one can judge their reliability and integrity. Many of these companies use a form of the word resveratrol in their names and sell only via a website. The lawyers for Dr. Mehmet Oz and Oprah Winfrey recently filed federal lawsuits against over 50 of these companies for illegally using their trademarks and making false claims that their products were endorsed by these well-known personalities. A copy of the litigation can be downloaded by visiting the following link:

http://www.scribd.com/doc/19144074/Harpo-Productions-versus-MonavieOprah-Dr-Oz-Suing-More-Than-50-Companies

A manufacturer rather than simply a reseller

Many suppliers buy raw material from Asian sources at the lowest possible price and simply fill capsules, rather then collect the plant and process it in their own GMP-certified facility. Legitimate resveratrol supplements will have passed Consumer Lab's recently updated evaluation of resveratrol brands, and its website should provide easy methods to contact the company if you have any questions, complaints or a request for a refund.

Ten years, preferably more, of ethical business operations with no unresolved Better Business Bureau complaints

It should offer a range of products not only one or two virtually identical products. If the company offers a monthly recurring order program a clear and convenient means of canceling your subscription should be offered. Before you give your credit card information to an on line seller be sure that the company is legitimate. This can usually be established by contacting your local BBB and doing a bit of on line due diligence.

The supplement is sold retail shops, not only through websites

If the company's products are not available in brick and mortar stores such as GNC, Walgreens, The Vitamin Shop and other reputable resellers it should probably be avoided. Anyone can sell a product over the Internet but to have one's products accepted by major Health and Supplement stores requires liability insurance, thorough testing of the products' quality and vetting of the company and its principals. Shops that carry supplements carry out thorough due diligence of both

the product itself and the company supplying and manufacturing the product. You have no such assurance with most online suppliers.

This is not to say that all online suppliers sell inferior quality supplements. There are some very reputable and ethical Internet merchants and manufactures. Unfortunately however, with any new supplement comes a raft of brand new suppliers with no history or experience in manufacturing advanced nutritional products who buy from lost cost, low quality brokers and whose products consistently fail independent evaluation. These companies usually employ highly unethical business practices or compete entirely on the basis of price. More often than not their products are virtually worthless, their customer service is nonexistent and their lifespan is measured in months if not weeks.

The gold standard is acceptance by the medical and research communities

The resveratrol brand used in human trials at institutions such as the Albert Einstein Medical School, Ottawa Hospital, Harvard, the University of Ferrara, University of Queensland in Australia and the NIH is by necessity the purest and most thoroughly tested supplements available to the general public. These institutions must put any product used in human trials through a rigorous and extensive series of tests for purity, potency and toxicity. Their endorsement is far more valuable than any test done by the manufacturers themselves or by the so-called independent labs.

One company whose products satisfy all of these criteria, and which have been used in National Institutes of Health, Health Canada and other health ministry-funded studies is Biotivia, who introduced the original resveratrol supplement over six years ago. The company has been in operation in the US and Europe for over 20 years.

On the opposite end of the scale are the companies who have sprung into existence to take advantage of the hundreds of news articles about resveratrol's potential health benefits. In mid-2010 Oprah Winfrey hosted Dr. Mehmet Oz on her program to talk about extreme life extension. He extolled the virtues of resveratrol in his presentation and shortly thereafter literally dozens of new suppliers materialized offering free bottles of resveratrol and claiming an endorsement by Dr. Oz. Not only were they deceiving customers with their sleazy marketing schemes, their products were found, in many cases, not to contain resveratrol at all. The lawyers for Dr. Oz and Oprah's production company filed suit against most of these companies, and the states' attorney general in several states launched criminal investigations. If you are interested in which brand was actually used by Dr. Oz in his presentation on the Oprah's show you can search for the term resveratrol on Dr. Oz' or Oprah's website.

Future Prospects

My prediction is that 'resveratrol will become both a stand-alone preventative agent and an effective treatment for a variety of human health conditions within five years. Perhaps more importantly, it will gain widespread acceptance as a co-treatment to be used to enhance the efficacy of existing drugs and non-drug treatments for a wide range of conditions. Finally, resveratrol will, within the next year, become a popular supplement and component in functional foods for its ability to improve the overall health and quality of life of those who choose to take advantage of it.

The preponderance of peer-reviewed published data now in the public domain elucidating the various benefits of resveratrol is very compelling evidence of resveratrol's importance to medical science and to con-

sumers concerned about improving and extending health and longevity. During this year and the next, a large number of human clinical trial results will be published by some of the world's most respected scientific institutions. I believe that virtually all of these studies will confirm the results and conclusions set forth in earlier in vitro and small-scale human clinical trials. If this turns out to be true it will be irresponsible of the medical community to fail to incorporate resveratrol into their recommended treatment modalities.

Medical ethicists set a very high standard for adoption of a new drug, treatment or technology. This standard is called the precautionary principal. One definition of this principle is set forth in a paper titled "The Precautionary Principle" authored by UNESCO's World Commission on the Ethics of Scientific Knowledge and Technology.

"When human activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish that harm."

So how does resveratrol stack up against this rigid standard? Given what we now know about resveratrol's ability to beneficially modulate so many biological processes, and its absence of any significant toxicity or adverse effects in the thousands of studies done to date, it is fair and reasonable to contend that resveratrol has met the first criterion of this standard. However this is only the first of two prerequisites which a new drug or treatment must satisfy to justify its adoption.

It is equally imperative that the treatment, drug or technology offers a legitimate benefit to its users or consumers that outweighs the foreseeable risks. Some level of risk is acceptable and inevitable. Every action we choose to take or to avoid entails risk. The precautionary principle simply states that risks must be reasonable when considered in light of the benefits. Resveratrol's benefits, if only judged in terms of its an-

tioxidant properties and the few human clinical trials to date, satisfies this second criterion as well. If I am correct, and the ongoing human clinical trials confirm resveratrol's safety and efficacy, not only will it have justified its adoption by the medical community, it will have established itself as a compound whose safety and importance to human health exceeds that of many of the pharmaceuticals commonly being used today to treat disease.

Scientific studies confirming statements and claims made in this publication.

Anti-inflammatory effects of resveratrol

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Cerebral blood flow and cognition

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