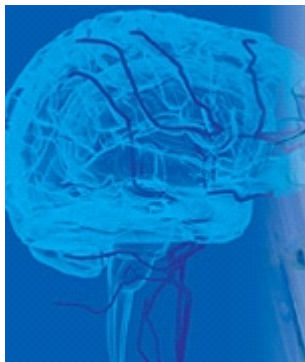


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## REPORT

### Nutrient 'Cocktail' Delays Aging and Extends Life Span

By Susan Machado



An international coalition of researchers has proved in the laboratory that a comprehensive 'cocktail' of nutritional supplements significantly increased youthful life span.<sup>1</sup>

Since aging is a multifactorial process with overlapping causes, scientists formulated a 30-ingredient nutrient mixture with overlapping benefits designed to halt or slow the major causes of aging.

The nutrient mixture, developed by a team of life scientists led by Dr. C. David Rollo of McMaster University in Canada, targets five key mechanisms of aging.<sup>1-3</sup> Researchers postulated that by slowing or reversing these five universal processes, they could slow or reverse the major factors of aging.

While this research was initially conducted on animals, every one of the 30 nutrients is already in human use as a supplement. All have established records of safety and effectiveness at promoting health and preventing specific disease processes. Many of the nutrients are already known to improve cognition, enhance mobility, slow aging, or extend life spans. Others have clear-cut beneficial effects on one or more of five key aging mechanisms, adding value to the combination as a whole.

The implications that this nutrient cocktail has on human longevity are profound.

Let's look now at these five fundamental causes of aging to understand the multiple ways that this nutrient mixture attacks them.

#### TARGETING FIVE KEY MECHANISMS OF AGING

Dr. Rollo's researchers recognized that, while aging is a complex phenomenon, most of its manifestations could be traced to a relatively small number of basic processes. Among these, there are five that account for most of the tissue, organ, and system dysfunction that produces chronic disease and untimely death. These five are well known to Life Extension® members: oxidative stress, inflammation, mitochondrial dysfunction, insulin resistance, and integrity of membranes.<sup>1-3</sup>

No single mechanism alone accounts for any one specific disease process. Instead, all five mechanisms interact with one another to produce both general aging and specific conditions that limit activity, cognitive function, and ultimately life span.

In developing a functional, multi-nutrient anti-aging formula, Dr. Rollo's group targeted the five key mechanisms of aging.

The scientists recognized that these specific mechanisms accounted for the vast majority of age-related, longevity-impairing conditions. In this way, the researchers cast a wide net to encompass as many disease states of aging as they could. Additionally, they chose laboratory mice to study the impact of the nutrients on aging because of the animals' short normal life span. This would help the researchers learn the most in the least amount of time. A mouse is considered 'old' by age 2 years, providing a convenient and realistic setting for the study of age-related conditions.<sup>3</sup> A human study might have taken decades before they could draw meaningful conclusions.

Next, the researchers needed to establish markers of progressive aging. They wanted to know not only how long the animals



lived, but also how well they functioned as they grew older. Most importantly, they needed measures that were equally applicable to both mice and to humans. Based on the work of others, Rollo's group decided that those criteria could be met by measuring how much the aging animals moved, and how their cognitive function changed with time.

## AGING, MOBILITY, AND COGNITION

All animals, from worms to insects to humans, change in very similar fashions as they succumb to the five key mechanisms of aging. In particular, changes in mobility and cognition provide reliable ways to measure the impact of aging on an individual's function.

As they grow older, all animal species move about less and less each day, spending more and more time at rest or in sleep.<sup>3</sup> Reduced mobility is an excellent marker of aging, because it is closely linked to overall metabolic rate, feeding, fat storage, brain neurotransmitter levels, mitochondrial function, and cardiovascular and skeletal muscle systems.<sup>3</sup> And loss of mobility in humans is associated with muscle wasting, bone thinning, and other changes that increase the risk of other negative outcomes such as fractures, pneumonia, and skin infections.

Cognitive function also declines with age in all animal populations. Younger animals typically learn faster, requiring fewer repetitions to master a task. They can also bring up important memories faster and more accurately, allowing them to find food, escape threats, and protect other members of their species. Studies show that preserving cognitive function into older ages is associated with longer life spans.<sup>2,4</sup>

Thus, by choosing to examine the animals' mobility and cognitive function, in addition to their longevity, Dr. Rollo's research group was able to measure how their mice were aging in ways that are likely to be applicable to humans as well.

Let's see how the mice did.

## RESULTS FROM ANIMAL STUDIES

After devising their 30-ingredient nutrient cocktail based on the five key mechanisms of aging, Dr. Rollo's group soaked the mixture into small pieces of bagel, which they then fed to the mice; control mice were fed only the bagel bits without the supplement.<sup>1-3</sup>

First, they determined the effect of the supplement on longevity. They used both normal mice and a special strain that demonstrates accelerated aging as a result of excessive sensitivity to all five aging mechanisms.<sup>1,5</sup> Compared with control animals, the supplemented mice of the accelerated aging strain lived **28%** longer.<sup>1</sup> Supplemented normal mice survived **11%** longer than their controls.<sup>1</sup>

Rollo's researchers then turned their attention to the animals' mobility as one measure of their general function with aging. They placed the mice in a system of transparent chambers, where they were given food, water, and an exercise wheel. Then they recorded the amount of time each animal spent moving about the enclosure over a 24-hour period.

Normal, unsupplemented mice showed a progressive decline in activity; by 24 months their mobility was roughly half that of younger normal animals. By 24 months of age, supplemented normal mice were moving roughly three hours more per day than were unsupplemented animals.<sup>3</sup> No other treatment has ever been found that ameliorates declining mobility to this extent.<sup>3</sup>

Rollo's group also measured biochemical markers that might explain the differences in mobility between supplemented and unsupplemented animals. Supplemented older mice had:

- n Increased activity of the neurotransmitter dopamine; decreased dopamine levels are associated with loss of movement in aging humans and in those with Parkinson's disease.<sup>3</sup>
- n Increased measures of mitochondrial activity, suggesting that supplemented animals simply had more energy as they aged.<sup>3</sup>
- n Decreased levels of protein carbonyls, altered molecules that reflect the impact of glycation and oxidation on cells and tissues.<sup>3</sup>

Taken together, the results of this study provided compelling evidence that the multi-nutrient mixture could slow down and perhaps even stop many age-related changes that contribute to the dangerous loss of mobility so common in older individuals.

Rollo's next study investigated the effects of the nutrient mixture on the cognitive decline that also threatens both quantity and quality of life as we age. Just as in the previous study, the researchers provided the nutrient mixture soaked onto bagel

pieces, giving control animals plain bagels.<sup>2</sup> Next, they tested the mice on a 'water maze' that required the animals to find and remember the location of a platform submerged just below the surface of a pool filled with water. This simple exercise, which tested the animals' learning skills as well as their memory, was repeated each day for five days.

As one might expect, on day 1 all of the mice had trouble finding the platform at first, taking an average of 81 seconds. By day 5, young mice had learned and remembered enough to find the platform **43%** faster than on day 1. Older unsupplemented mice, however, showed no significant improvement in the time it took them to find the platform, indicating age-related impairments in learning and memory.

But with supplementation, old mice showed a level of learning almost identical to that of young mice; in fact on day 5 they took an average of **46%** less time to find the platform than they did on day 1. In other words, supplemented old mice showed the same ability to learn and remember new tasks as did young animals (See figure 1).

As with their previous study, Rollo's researchers also sought biochemical and structural explanations for the observed improvements in the supplemented animals' behavior. They found that:

- n Brain mitochondrial activity fell steadily with age in the untreated mice, while supplemented animals showed a steady increase in this important measure of brain energy supply.<sup>2</sup>
- n Mice with higher brain mitochondrial activity proved to be significantly better learners than those with lower mitochondrial activity.<sup>2</sup>
- n Brain weights, which normally decrease with age, were higher in supplemented male mice by **7%**, and in females by **11%**, compared with brain weights of control animals.<sup>2</sup>

Together, Rollo's findings present a remarkable picture of our emerging ability to control not one, but five of the key pathways to an aging body and mind. In their papers, the researchers freely admit that they don't yet have precise knowledge of exactly how each nutrient is working in their experimental model.<sup>1-3,5</sup> But they recognize the great importance of addressing multiple aging pathways each through multiple mechanisms.

And there is no paucity of evidence that each of the 30 nutrients in the mixture has powerful, and often multiple, effects on the aging process, as shown in the next section.

## WHAT YOU NEED TO KNOW: DELAY AGING AND EXTEND LIFE SPAN

- n Aging is a complex, multifactorial process, but five major mechanisms are now known to account entirely or in part for most human age-related diseases, and to contribute to the aging process itself.
- n Scientists from Canada and China have devised a 30-nutrient supplement mixture designed to attack all five mechanisms of aging by multiple pathways.
- n Tested in mice, the supplement mix extends life span by up to **28%** while improving the aging animals' mobility and cognitive function.
- n All 30 nutrients are known to be safe and effective in human beings.
- n If this mixture, or one like it, has similar effectiveness in humans, one could expect an 80-year-old to add nearly **9 years of life**, with youthful levels of activity and cognition.



## INGREDIENTS SYNERGIZE TO SLOW AGING, ENHANCE COGNITION, BOOST MOBILITY

Rollo's group of researchers chose nutrients with known abilities to attack five of the key mechanisms of aging. As shown in the Table of Ingredients, the majority of the ingredients have more than one mode of action on more than one of the major mechanisms of aging. This kind of multitargeted activity is a hallmark of nutritional supplements. The fact that the formula contains many multitargeted nutrients with overlapping mechanisms of action may underlie its dramatic effects. Such characteristics are typically lacking in prescription drugs, which generally target only one mechanism, and when they interact it is often in a negative, rather than a synergistic fashion.

The nutrient mixture's ingredients have individually been shown to have powerful disease-fighting, health-promoting effects. Those effects, like the ones demonstrated in Dr. Rollo's series of studies, promise not only to increase longevity, but also to promote healthy mobility and preserve youthful cognitive function. Here is a summary of the impact these effects have on real-life human aging:

Antioxidant nutrients protect brain cells, slow brain aging, and reduce memory impairment, while also lowering cardiovascular and metabolic disease risks, preventing cancer, and improving immune function.<sup>6-18</sup>

Ingredients with anti-inflammatory actions protect against neurodegenerative diseases, improve cardiovascular and endothelial function, prevent fatty liver disease, improve muscle function, and fight cancer.<sup>14,19-33</sup>

The mitochondrial-enhancing nutrients improve energy availability in many tissues, preventing fatty liver disease, promoting weight loss and preventing obesity, improving cardiovascular and skeletal muscle function, improving cognition, and protecting brain cells from Parkinson's disease.<sup>34-47</sup>

Nutrients that overcome insulin resistance further aid in normalizing energy utilization, enhancing cognitive function, preventing metabolic syndrome from emerging, improving glucose and insulin responses during exercise, while of course lowering acute and chronic blood glucose, reducing hemoglobin A1C levels, and delaying complications of diabetes.<sup>48-59</sup>

Finally, nutrients that preserve membrane integrity improve cell-to-cell signaling and protect cellular DNA, improving brain cell and muscle function, inducing cancer cell death, protecting against atherosclerosis and slowing progression of cardiovascular disease, enhancing muscle health, and protecting liver cells.<sup>34,60-72</sup>

As you can see, this is an exhaustive list of preventive actions, many of which overlap. That, of course, is one of the desirable features of this formulation: aging is a complex, multifactorial process with overlapping causes, so preventing it requires a multitargeted approach using overlapping mechanisms.

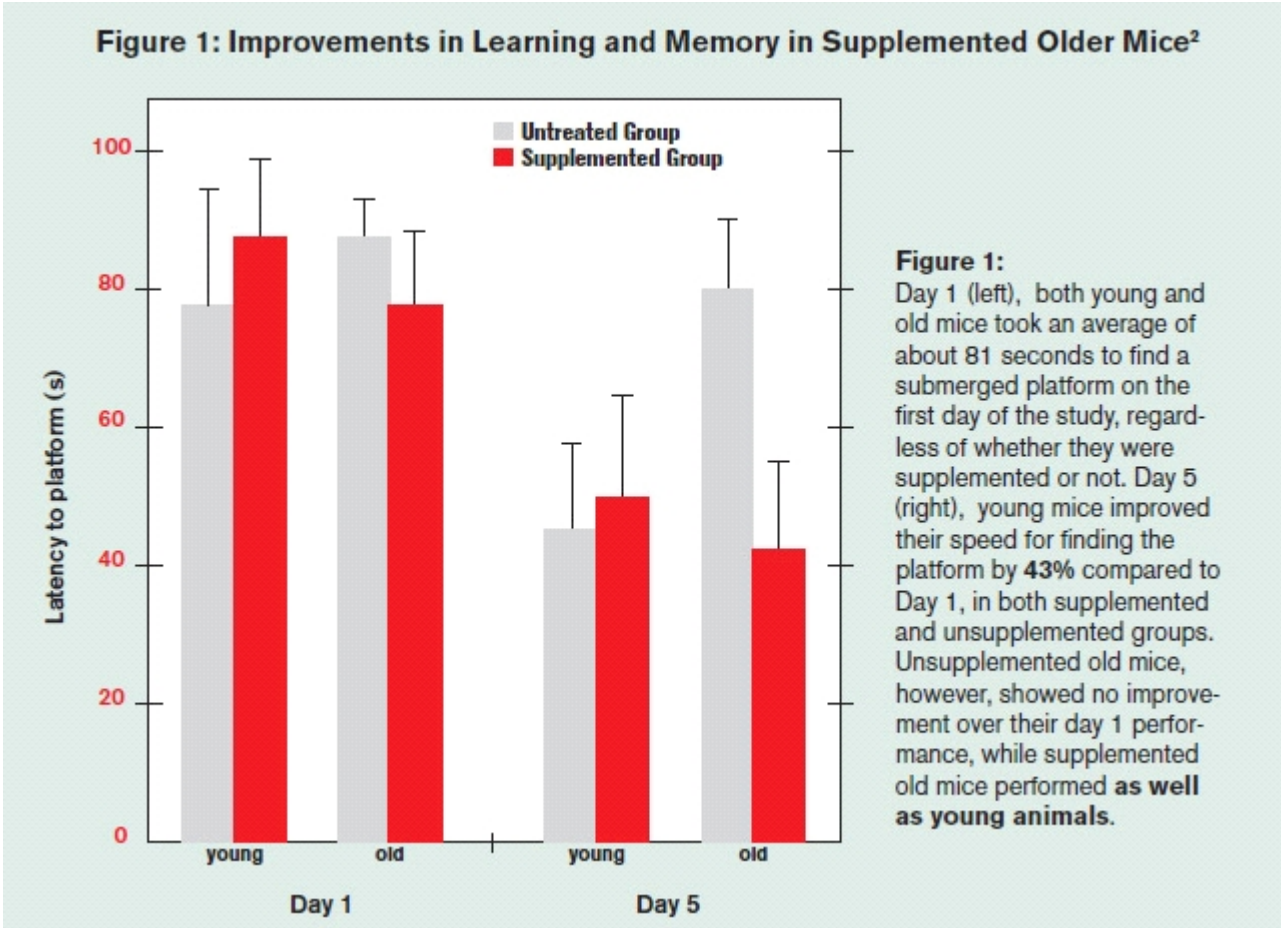


TABLE OF NUTRIENT COCKTAIL INGREDIENTS					
Nutrient	Mechanisms of Aging Affected				
	Oxidant Stress	Inflammation	Mitochondrial Function	Insulin Resistance	Membrane Integrity
B Vitamins (Vitamins					

B1, B3 (niacin), B6, B12) and Folate	X <sup>124</sup>		X <sup>73</sup>	X <sup>125</sup>	
Vitamin C	X <sup>74</sup>				
Vitamin D		X <sup>75,76</sup>		X <sup>77,78</sup>	
Acetyl-L-carnitine	X <sup>126</sup>		X <sup>45-47</sup>		
Alpha-lipoic acid	X <sup>128,130</sup>	X <sup>127</sup>	X <sup>44,131</sup>	X <sup>128-130</sup>	
Acetylsalicylic acid (aspirin)		X <sup>79</sup>			
Beta-carotene				X <sup>80</sup>	X <sup>65</sup>
Bioflavonoids	X <sup>13</sup>	X <sup>81</sup>			
Chromium picolinate				X <sup>49,82,83</sup>	
Garlic	X <sup>132</sup>	X <sup>84</sup>		X <sup>85</sup>	X <sup>64,86</sup>
Ginger root extract	X <sup>14,87</sup>	X <sup>14,58</sup>	X <sup>133</sup>	X <sup>57,88,89</sup>	X <sup>134</sup>
Ginkgo Biloba	X <sup>90-92</sup>				
Ginseng	X <sup>93</sup>	X <sup>59</sup>	X <sup>94-96</sup>	X <sup>94,95</sup>	X <sup>96</sup>
Green tea extract	X <sup>97</sup>	X <sup>21,98,99</sup>		X <sup>100,101</sup>	
L-Glutathione	X <sup>102</sup>				
Magnesium	X <sup>103,104</sup>			X <sup>105-107</sup>	
Manganese	X <sup>108</sup>			X <sup>109,110</sup>	
Melatonin	X <sup>7</sup>	X <sup>111,112</sup>			
N-Acetyl cysteine	X <sup>113</sup>				
Potassium	X <sup>114</sup>			X <sup>114</sup>	
Rutin	X <sup>115</sup>	X <sup>116</sup>			
Selenium	X <sup>117</sup>	X <sup>118</sup>	X <sup>135</sup>	X <sup>51,52</sup>	X <sup>70</sup>
Vitamin E	X <sup>74,119</sup>				
Cod liver oil (omega-3)		X <sup>120</sup>			X <sup>121</sup>
Coenzyme Q10	X <sup>136</sup>	X <sup>137</sup>	X <sup>42</sup>		
Flax seed oil		X <sup>122</sup>			X <sup>123</sup>

**TABLE:** A total of 30 nutrients provides comprehensive coverage of all five key aging mechanisms. Note that most nutrients have multiple functions, and that all five mechanisms are addressed by multiple nutrients.

Growing scientific evidence connects most of the chronic diseases, and even longevity itself, with five key mechanisms of aging.

By devising a supplement formula comprised of multiple nutrients that attack these five mechanisms through multiple pathways, international researchers have significantly lengthened the life span of experimental animals. Just as importantly, the nutrient mixture markedly enhances animals' overall mobility and cognition, restoring function in those areas to youthful levels.

The marked benefits demonstrated in response to this 30-ingredient nutrient cocktail help explain why studies with single-agent compounds do not always produce meaningful longevity-enhancing results.

All of the individual nutrients in the mixture are known to be safe and effective in humans, though time will tell if the specific combination of all thirty will prove as effective in humans as it has in mice. The preponderance of the evidence, however, suggests it may live up to expectations.

If you have any questions on the scientific content of this article, please call a **Life Extension®** Health Advisor at 1-866-864-3027.

## THE 30 NUTRIENTS USED IN THIS HEALTH AND LONGEVITY STUDY

Vitamin B1	Ginkgo biloba
Vitamin B3 (niacin)	Ginseng
Vitamin B6	Green tea extract
Vitamin B12	L-Glutathione
Folate	Magnesium
Vitamin C	Manganese
Vitamin D	Melatonin
Acetyl-L-carnitine	N-Acetyl cysteine
Alpha-lipoic acid	Potassium
Acetylsalicylic acid (aspirin)	Rutin
Beta-carotene	Selenium
Bioflavonoids	Vitamin E
Chromium picolinate	Cod liver oil (omega-3)
Garlic	Coenzyme Q10
Ginger root extract	Flax seed oil

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