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Careless®

... the innovation for well-aging

By Christina Ehrhardt and Dr. Sybille Buchwald-Werner
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The world's population is aging rapidly. According to the WHO, the proportion of people over 60 years is expected to increase from 605 million to 2 billion between 2000 and 2050 [1]. In parallel, life expectancy is rising.

Aging is associated with several structural and metabolic changes leading to a decrease in physical strength and endurance as well as to a decline in efficiency of body organs and a shift of body composition towards an increase in body fat mass. Many of these changes occurring from aging result from a gradual loss that often begins already around the age of 30 years.

Today's aging consumers are thought to be the physically and mentally fittest in history. Young and old take personal responsibility for their health and are interested in measures to reduce the signs of aging and the risk of metabolic diseases that tend to strike as we age. Besides establishing lifestyle changes, consumers are looking for natural, safe alternatives to support their goal of lengthening their "healthy life expectancy", i.e. the number of years in "full health". Today, there is a difference of at least seven years between the "healthy life expectancy" and total life expectancy at birth [2]. Thus, products helping the aging consumer to close this gap between healthy life expectancy and total life expectancy may have a huge potential.

Careless® is a well-tasting, innovative and IP protected ingredient that helps you care less about aging by mimicking some of the effects of calorie restriction and exercise, two well-known measures to stay healthy and in shape.

Mango – "the king of fruits" – traditional use and efficacy

What is Careless? Careless is a high quality mango fruit preparation with excellent taste providing a good basis for healthy food and dietary supplement concepts. Mango (*Mangifera indica L.*) is one of the most important tropical fruits, grown in more than 87 countries throughout the world [3]. It is not only a delicious fruit consumed at every stage of ripeness but also known for its traditional health benefits. Various parts of the plant (e.g. roots, bark, leaves, kernel) are used in Ayurvedic medicine to treat a broad spectrum of diseases including diarrhea, diabetes, liver diseases and many more [4].

The fruits of mango are known to contain significant levels of bioactive compounds including polyphenols and vitamins. The composition and concentration of bioactives is influenced by several factors such as genetic differences in cultivars, growing conditions,

ripeness and post-harvest handling [4, 5]. Mango polyphenols are highest during fruit growth and decrease with ripening. Analytical investigations of unripe fruits displayed even higher contents of polyphenols in unripe fruits.

The mango fruits used for Careless are harvested at a special degree of ripeness in order to ensure a high concentration of bioactive compounds. The use of unripe fruits also has technological advantages. The firm pulp can be sliced easily and dried under moderate conditions to produce a high quality fruit powder without deterioration of valuable compounds and related beneficial effects or of the great color and taste.

Secondary plant compounds such as polyphenols have been increasingly researched for their health benefits in particular with regard to the prevention of age related and metabolic diseases. For this reason, Vital Solutions Swiss AG has started a research program elucidating the benefits of Careless for well-aging.

As we age, the function mitochondria, the power plant of cells, declines leading to disturbances in energy homeostasis, metabolism, and proper cell viability.

Emerging research revealed that energy homeostasis and related metabolic processes are steered by the evolutionary conserved metabolic sensors Sirt-1 (sirtuin-1) and AMPK (5'AMP-activated protein kinase) which respond to the increase in cellular AMP (adenosine monophosphate) and NAD⁺ (nicotinamide adenine dinucleotide) concentrations. During exercise (energy depletion) or calorie restriction (lack of energy), Sirt-1 and AMPK are activated and hence stimulate a cascade of metabolic processes that "instruct" the body to start burning energy and stop storing it. AMPK activation results e.g. in increased fatty acid oxidation, inhibition of cholesterol, fatty acid and triglyceride synthesis, enhanced muscle glucose uptake and modulation of insulin secretion [6, 7]. Sirt-1 stimulates similar processes related to glucose, insulin and lipid metabolism as well as those related to increased stress resistance (see Figure 1) [8]. Together these players are suggested to explain many of the beneficial effects of physical activity and dietary interventions known to improve metabolic fitness as well as to help prevent metabolic diseases [9].



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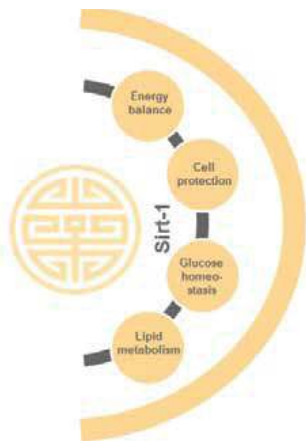


Figure 1: Suggested metabolic benefits related to Sirt-1 activation.

Careless has recently been shown *in vitro* to activate both Sirt-1 and AMPK underlining the potential of the ingredient for well-aging concepts. Besides its beneficial effects on key energy sensors, Careless has anti-inflammatory properties as demonstrated by an attenuation of the release of inflammatory cytokine interleukin-6 (IL-6) in macrophages. Moreover, Careless has inhibited cyclo-oxygenase 1 an enzyme responsible for the formation of prostaglandins and thromboxanes. Inflammation as a function of aging has been well characterized in numerous epidemiological studies. Levels of inflammatory mediators increase with age even in the absence of acute infection or physiologic stress. Multiple inter-related mechanisms contribute to age-related inflammation with oxidative stress being one stimulator of chronic inflammation. Careless does not only have a good anti-oxidative capacity but may also contribute to an improved oxidative stress resistance via its Sirt-1 activating effects. Sirt-1 is known to stimulate the expression of anti-oxidants and to inhibit NF- κ B signaling, a major inducer of inflammatory responses [6].

Last but not least, the potential of Careless to activate Sirt-1 and AMPK may contribute to the promotion of health during aging by supporting mitochondrial biogenesis. Sirt-1 and AMPK have been shown to stimulate PGC-1 α , a master regulator or mitochondrial biogenesis [9]. Effective mitochondrial biogenesis and turnover is critical for the maintenance of energy production, the prevention of oxidative stress and well-aging [10]. In muscle cells for instance, mitochondrial biogenesis is related to improved muscle aerobic capacity, endurance and muscle mass [11].

In all, interventions that maintain or improve the activity of AMPK and Sirt-1 may help prevent the deleterious changes of aging including negative changes in body composition, reduced physical energy, and increased risk for chronic diseases such as type 2 diabetes and cardiovascular disease. Careless is a promising candidate to positively affect

well-aging by stimulating exactly these key metabolic sensors.

Technological aspects

Careless is a high quality, sustainable, fine yellowish powder obtained from mango fruit, *Mangifera indica* L.. The production facility and manufacturing process complies with the highest international standards of safety, hygiene and quality control: ISO-9001:2008, ISO-22000:2005. Due to its fruity taste and brilliant yellow-orange color, Careless can be nicely used as functional ingredient in foods and food supplements including non-masking formulations like chewing gums which provide to consumers the healthy element in combination with a great food experience.

Conclusion and outlook

Careless is a natural, IP protected healthy innovation for well-aging products. Based on *in vitro* evidence, Careless may help attenuate the negative metabolic changes associated with aging while delivering the pleasure and taste of exotic mango. The metabolic and anti-inflammatory effects of Careless benefit consumers at any age and suggest product concepts not only for the maintenance of muscle mass and physical energy, but also for the reduction of the risk for metabolic age-associated diseases, as well as cell protection.

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Healthful ingredients

... that address the major health concerns of aging consumers

By Michelle Braun, Sr. Research Investigator - Protein Solutions

In 2013, over 2.5 billion people worldwide were aged 40+ years. That number is projected to reach 3.5 billion by 2030, representing 42 percent of the population¹. The fastest growing sector will be aged 60+ years, as the segment of the population aged 40+ years continues to rise¹. Today's aging consumer comes in many shapes and sizes. Therefore, marketing to consumers based on age alone will not lead to success. It is essential to appeal to consumers in this age bracket based on their needs, not based on a number alone.

Many of these consumers prefer the use of foods and drinks that enhance their health over medications. In fact, there is a distinct opportunity within a sub-segment of this age group who have high nutritional awareness, are highly motivated to change, have health concerns and are looking for food, beverage and supplements to help. Meeting the nutrition needs of these early adopters who select foods and beverages to promote health as well as motivating them to action is vital.

As the population ages, the prevalence of overweight and obesity is also increasing, globally. The World Health Organization predicts there will be 2.3 billion overweight adults in the world by 2015 and more than 700 million of them will be obese². A recent analysis of the National Health and Nutrition Evaluation Surveys (NHANES) data indicated that in the US in 2010, an estimated 73.5 percent of all women and 76.5 percent of all men aged 60 years or older were either obese or overweight, exceeding the average rate (69.2 percent) for adults of all age groups³. Aging is associated with body composition changes, with a tendency towards increased adiposity and decreased lean body mass⁴.

Dietary strategies for increasing satiety for weight management

In most weight loss studies or programs, people are able to lose some weight with calorie restricted diets but many experience hunger pangs because they may not be given adequate macronutrients to support satiety, or the feeling of fullness, associated with the delay in consumption of the next eating occasion. Strategies for weight management also affect gut hormones as potential targets for metabolic appetite regulation⁵. There is also the need to lose abdominal fat, which is the biologically active fat linked to metabolic disorders such as diabetes and metabolic syndrome. An additional factor during weight loss and weight management is the need to maintain lean body mass, including muscle tissue. Losing muscle may equal greater weight loss, but in the long run the loss of muscle will lead to other issues such as decreased strength and mobility, a key area of concern among aging adults.

Both fiber and protein are integral parts of foods to support weight management. Dietary protein and fiber can affect appetite, promote satiety, and ultimately serve as valuable nutrients for healthy weight management.

Fiber intake has been associated with satiety and less weight gain. Dietary fiber can increase satiety and reduce short-term energy intake largely in part by adding bulk to foods, thereby reducing its energy density. Fiber-containing foods may also increase satiety by requiring the individual to spend more