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Health Research & Studies Center

# **Health Benefits of**

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# **Sun-Dried Raisins**

Review of the Scientific Literature

2012

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# Health Benefits of Sun-Dried Raisins

## Prepared For:

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## Executive Summary

Raisins are naturally endowed with both an array of valuable nutrients and a pleasantly sweet flavor. Raisins as part of the daily diet provide essential nutrients, soluble and insoluble fiber and a unique composition of health protective bioactive compounds, or phytochemicals.

- ❖ Raisins, like other fruits, are devoid of fat, saturated fat and cholesterol.
- ❖ Raisins, like all fruits, are high in potassium and low in sodium. Compared to other fruits, they are high in magnesium and iron. Raisins are among the richest sources of boron in the American diet.
- ❖ Both raisins and grapes provide similar amounts of sugar, divided almost equally between fructose and glucose with minimal amounts of sucrose.
- ❖ Diets high in dried fruits are associated with lower BMI, reduced overweight and abdominal obesity and improved diet quality using NHANES (1999-2004) data. Moreover, new research suggests eating raisins as an after-school snack prevents excessive calorie intake and increases satiety - or feeling of fullness - as compared to other commonly consumed snacks.
- ❖ Raisins may promote healthy teeth and gums. Contrary to popular perception that raisins promote cavities, studies show that phytochemicals found in raisins may benefit oral health by fighting bacteria that cause cavities and gum disease. Raisins also exhibit rapid clearing rates, placing them among the least retentive foods within a sample of snack foods. Finally raisins contain minimal amounts of cariogenic sucrose.
- ❖ Raisins provide both soluble and insoluble fiber at levels that represent a meaningful contribution to daily fiber intake. High fiber diets are recommended to reduce the risk of developing various conditions, including constipation, heart disease, diabetes, diverticular disease, colon cancer and obesity. The Institute of Medicine and the Dietary Guidelines for Americans 2005 recommend 14g of fiber for every 1,000 calories of food consumed each day. However, most Americans eat far less fiber than this. Adding raisins to a daily diet helps meet dietary fiber requirements.

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- ❖ Raisins are a source of prebiotic compounds in the American diet. Raisins provide fructooligosaccharides (fructans) including inulin. Formed from grape sugars during dehydration, fructans in raisins may help regulate bowel functions and stimulate health-promoting intestinal flora, maintaining intestinal balance and colonic health.
  - ❖ Raisins are a major dietary source of tartaric acid, a fruit acid that is fermented by colonic bacteria and has been shown to have a beneficial role in intestinal function. Tartaric acid may act synergistically with fructans to enhance the potential of raisins as a prebiotic food. Tartaric acid enhances mineral absorption from foods. Raisins paired with iron-fortified cereals will enhance iron absorption.
  - ❖ Raisins are rich in polyphenols: flavonoids and phenolic acids. These bioactive compounds have a multitude of functional capabilities that may have a health protective effect. Polyphenols may be responsible for the health benefit associated with the consumption of diets abundant in fruits and vegetables. Health agencies around the world recommend that populations increase their daily fruit and vegetable intake but a significant gap still remains between the amount of fruits and vegetables recommended and the quantities Americans eat. Raisins are a convenient means to bridge this gap.
  - ❖ Because of their high phenolic content, raisins are an important source of antioxidants in the diet. In terms of their antioxidant capacity raisins are ranked within the highest quartile among fruits and vegetables. Raisins have been shown to raise blood antioxidant capacity in healthy adults and to protect against oxidative damage to critical cellular components.
  - ❖ Raisins, like other fruit, may help protect from cardiovascular disease. Raisins are a good source of fiber (soluble and insoluble), potassium and polyphenols, food components are important for cardiovascular health. Raisins, as part of a diet high in whole and unrefined foods, have a beneficial effect on lipid levels. The addition of raisins to the a daily diet has been shown to lower total and LDL cholesterol levels, reduce markers of inflammation, increase plasma antioxidant capacity and lower

circulating levels of oxidized LDL, a marker of coronary heart disease risk. Regular snacking on raisins may promote healthy blood pressure.

- ❖ Raisins, like other fruit, may help protect from chronic diseases like cancer. Diets high in fruits and vegetables have been associated with a lower risk of developing cancer. Scientists believe that it is the additive and synergistic effect of phytochemicals in fruits and vegetables that are responsible for their health protective effect. Raisins, with their unique combination of nutrients, polyphenols and fiber are important ingredients of a dietary strategy for optimal health.
- ❖ The American Dietetic Association lists raisins among “The Perfect Snack”; foods that provide energy and also help meet nutritional needs. This is particularly important in a child’s diet since a mid-morning and a mid-afternoon snack should be an opportunity to increase a child’s intake of nutritious foods like fruits.
- ❖ The Committee on Nutrition Standards for Foods in Schools has designated raisins as a Tier 1 Food, foods that “provide important health benefits that warrant encouraging consumption by school-age children, and do not exceed levels of certain nutrients and compounds that may be unhealthful for school-age children when consumed in excess”.
- ❖ Raisins have a low Glycemic Index – a measure of how a food affects blood sugar levels. Coupled with their high antioxidant activity and fiber content, a moderate GI makes raisins a useful food in diabetes management. Raisins feature prominently in recipes promoted by the American Diabetic Association.
- ❖ Raisins, an excellent source of carbohydrates with a low GI food, are the ideal pre-exercise snack to provide sustained energy and ensure optimal athletic performance. Raisins have been shown to maintain steady glucose levels and support the demand for energy during sports activities.

## Summary of Sun-Dried Raisin Components of Physiologic Interest

| Component  | Bioactive Classification    | Potential Benefit <sup>†</sup>   |
|--|-----------------------------|--|
| <b>Boron</b>   | Mineral                     | <ul style="list-style-type: none"> <li>• Supports growth of healthy bones</li> <li>• Maintains healthy bones and joints</li> </ul>   |
| <b>Fiber, including Pectin</b>                       | Non-digestible carbohydrate | <ul style="list-style-type: none"> <li>• Colon cancer protection</li> <li>• Cholesterol lowering</li> <li>• Protection from cardiovascular disease</li> <li>• Support of colon health and function</li> </ul>  |
| <b>Pectin</b>  | Non-digestible carbohydrate | <ul style="list-style-type: none"> <li>• Cholesterol lowering</li> </ul>   |
| <b>Fructans</b>                                      | Prebiotic                   | <ul style="list-style-type: none"> <li>• Stimulation of health-promoting colonic microflora</li> <li>• Support of colon health</li> <li>• Stimulation of calcium and magnesium absorption</li> <li>• Colon cancer protection</li> </ul>                                    |
| <b>Tartaric acid</b>                                 |                             | <ul style="list-style-type: none"> <li>• Support of colonic health and function</li> <li>• Enhance mineral absorption</li> </ul>   |
| <b>Flavonols<br/>(e.g. quercetin and kaempferol)</b> | Flavonoids<br>(Polyphenols) | <ul style="list-style-type: none"> <li>• Antioxidants, protection from oxidative stress</li> <li>• Cardiovascular disease protection</li> <li>• Cancer protection</li> <li>• Anti-inflammatory</li> <li>• Protection from age-related neurological degeneration</li> </ul> |

<sup>†</sup> In many cases, research is still in preliminary stages.

|   |                                 |  |
|---|---------------------------------|--|
| <b>Hydroxycinnamic acids and derivatives</b><br><b>(e.g. caftaric and coutaric acids)</b> | Phenolic acids                  | <ul style="list-style-type: none"> <li>• Antioxidants, protection from oxidative stress</li> <li>• Cancer protection</li> <li>• Anti-inflammatory</li> </ul>   |
| <b>Isoflavones:</b><br><b>Daidzein and genistein</b>                                      | Phytoestrogens<br>(Polyphenols) | <ul style="list-style-type: none"> <li>• Antioxidants, protection from oxidative stress</li> <li>• Cancer protection (breast, prostate, colon)</li> <li>• Cardiovascular disease protection</li> <li>• Osteoporosis protection</li> <li>• Alleviate menopausal symptoms</li> </ul> |
| <b>Betulin, oleanolic and betulinic acids</b>   | Triterpenes                     | <ul style="list-style-type: none"> <li>• Anti-cavity, gum disease protection</li> </ul>  |

## I. Introduction

Raisins are naturally endowed with both an array of valuable nutrients and a pleasantly sweet flavor. Raisins as part of the daily diet provide essential nutrients, soluble and insoluble fiber and health protective bioactive compounds, or phytochemicals. This combination of nutritional bounty and enjoyable taste is the reason raisins have been popularly considered a healthy food for millennia. Raisins' natural resistance to spoilage and ease of storage and transport only serve to strengthen their appeal and widespread consumption.

The relationship between diet and health has been recognized since ancient times. Until as recently as the early 20<sup>th</sup> century, physicians prescribed specific foods and diets as remedies for illness and for their disease preventive value. Over the last 30 years food and nutrition research has focused on the role of certain foods and diets in lowering the risk of degenerative and chronic disease, and nutritionists have broadened their understanding of what makes up an optimal diet: one that does more than simply just provide sufficient nutrients to sustain growth and reproduction, but also promotes health and longevity and lowers disease risk. While the composition of an adequate diet is widely known and agreed upon, that of an optimal diet remains elusive.

Recent research suggests that diets largely based on plant foods, such as the Mediterranean diet, may be the best model to follow. Epidemiological studies have shown a consistent, inverse relationship between a diet rich in fruit and vegetables and a lower risk for many chronic diseases including cancer,<sup>1 2 3</sup> heart disease<sup>4 5</sup> and stroke.<sup>6</sup> Researchers are also investigating the beneficial role of fruits and vegetables in inflammatory diseases<sup>7</sup> such as arthritis; in lowering the incidence of obesity and controlling diabetes;<sup>8 9</sup> and in age-associated neurological problems such as Alzheimer's and Parkinson's Disease.<sup>10 11</sup> Fruits and vegetables also appear to have a role in the prevention of cataracts and macular degeneration,<sup>12</sup> and may also protect from osteoporosis.<sup>13</sup> Finally, they may enhance the immune system and potentially modulate certain aspects of immune function. The protective effect of an abundance of fruits and

vegetables in the diet is long lasting. Higher intake of fruits<sup>14</sup> and vegetables<sup>15</sup> during childhood is associated with a lower incidence of cancer and stroke, respectively, during adulthood.

The strength of the association between fruit and vegetable consumption and health has led organizations around the world to recommend that populations increase their daily fruit and vegetable intake. In the United States, dietary guidelines issued since 1977 by health agencies have vigorously endorsed and promoted this message.<sup>16</sup> In 1982, the National Academy of Sciences published a report on diet and cancer that emphasized the importance of fruits and vegetables in the diet.<sup>17</sup> In 1989, they expanded their message in another report, *Diet and Health*, which promoted the consumption of at least 5 servings of fruits and vegetables per day in order to reduce risk of both cancer and heart disease.<sup>18</sup> In 1991, the National Cancer Institute started the national "5 A Day for Better Health" program (Produce for Better Health, PBH), which called for 5 or more daily servings of fruits and vegetables. In 2003, the recommendations were expanded to encourage people to eat from 5 to 9 servings a day: "Eat 5 to 9 A Day for Better Health".<sup>19</sup> The most recent Dietary Guidelines for Americans, published by the United States Department of Agriculture (USDA) in 2005, recommends that adults eat 7 to 13 servings, according to their caloric expenditure, and children eat 4 to 10, depending on their age.<sup>20</sup> This has prompted the new message: "Fruits & Veggies – More Matters," beginning in early 2007.<sup>21</sup>

Despite these campaigns and educational efforts, Americans' fruit and vegetable consumption has not increased during the past two decades.<sup>22</sup> A significant gap still remains between the amount of fruits and vegetables recommended by the USDA and PBH campaigns and the quantities Americans actually eat. Looking at fruit intake specifically, in the period from 1988 to 1994 only an estimated 27% of adults met the USDA guidelines of two servings or more.<sup>23</sup> From 1999 to 2002, only 28% of adults met these guidelines. During the past 15 years, reports put the mean fruit daily intake at 1.8,<sup>24</sup> 1.4<sup>25</sup> and 1.2<sup>26</sup> servings (including fruit juices) for 4 to 5 year olds, 11 to 18 year olds and adults, respectively. Clearly, American eating patterns have yet to reflect an appreciation for the benefits of a diet rich in fruits.

Fruits and vegetables are not only important sources of vitamins, minerals and fiber in the diet but also provide a wide array of bioactive components or phytochemicals. These plant compounds are not designated as traditional nutrients since they are not essential to sustain life, but play a role in health and longevity and have been linked to a reduction in the risk of major chronic diseases. It is estimated that more than 5,000 individual phytochemicals have been identified but a large percentage still remain unknown. Convincing evidence suggests that the benefits of phytochemicals in fruits and vegetables may be even greater than is currently understood, since they affect metabolic pathways and cellular reactions believed to be involved in the etiology of a wide range of chronic diseases. However, the precise mechanisms by which specific compounds exert their observed biological effects remain largely hypothetical and are thus still the subject of intense investigation.

*Raisins should be of particular interest in these investigations due to their unique phytochemical composition and the natural qualities that make raisins an appealing source of nutrients. Raisins, like other fruits, are devoid of fat, saturated fat and cholesterol. They provide both soluble and insoluble fiber at levels that represent a meaningful contribution to daily fiber intake and at levels that benefit cardiovascular health. They are a source of fructooligosaccharides (fructans), which act as prebiotics, contributing to colonic health, and are a major dietary source of tartaric acid, a fruit acid that is fermented by colonic bacteria and has been shown to have a beneficial role in intestinal function. In the American diet, raisins are also among the richest sources of boron, a recognized essential trace element that may have an important role in bone health.*

*It is in their phenolic content, however, where raisins may prove to have the most important health effect. Raisins are rich in phenolic compounds: flavonoids and phenolic acids. Flavonoids are not only potent antioxidants but also have a multitude of functional capabilities, which may have an effect on health. Raisins provide the flavonoids quercetin, kaempferol and rutin, and are among the richest fruit sources of the isoflavones daidzein and genistein. Raisins are also a good dietary source of the phenolic acids caftaric and coutaric*

*acids. By virtue of their antioxidant activity, these raisin constituents may lower oxidative stress in humans and thereby lower risk of chronic disease.*

*Raisins are a fruit rich in cultural and nutritional value that may offer a convenient step toward healthier eating and a means to bridge the gap between recommended intake of fruits and the amount Americans actually consume. The raisin's unique flavor and nutritional qualities are reaffirmed by its prevalence throughout human history. Wherever viticulture flourished, it seems, raisins soon followed, and they eventually became popular in countless cultures and societies around the world. Even in areas where the climate did not support the sun-drying process, raisins were imported and included in local cuisines.*

## **II. Etymology**

The term “raisin” dates back to its use in Middle English, having been borrowed from Old French. In French, the word **raisin** actually refers to fresh grapes, whereas **raisin sec**, literally translating to “dry grape,” refers to the raisin. The French word itself comes from the Latin term **racemus**, meaning “a bunch of grapes.”<sup>27</sup>

## **III. Why Raisins**

Since ancient times, raisins have been valued as a form of preserving grapes so they would last through the winter months and could be more easily stored and transported.<sup>28</sup> Grapes were considered to be a nutritious and healthful food and raisins a good source of energy because of their high sugar content. Sun drying was seen as a natural way to produce raisins that not only gave them a particular intense flavor, but also maintained the delicate balance of nutrients of the original fruit. Some saw this age-old process as an extension of the natural ripening cycle of the grape. Indeed, it is almost certain that raisins and grapes occurred naturally before men intended to cultivate them.

## IV. Raisins in World History

The consumption of grapes and raisins, in particular, dates back to prehistoric times. Wild grapes existed as far back as 35,000,000 BC, when the species *Vitis sezoneensis* was known to grow in what is now southern France.<sup>29</sup> Hunter-gatherers likely recognized the healthful qualities of wild grapes and may have noticed that grapes took on an edible dried form after having fallen off the vine and lain in the sun.<sup>30</sup> Following this natural example, grapes were probably dried for storage and travel in the Neolithic period, leading to the early production of raisins.<sup>30</sup> There is evidence of early use of raisins as food and decorations, from prehistoric murals in the Mediterranean region to Bronze Age archaeological finds at Lachish in Israel.<sup>31</sup>

Grape cultivation first began in Armenia and the eastern regions of the Mediterranean, including ancient Phoenicia and Persia. Grapes were also important in Anatolia, where the Hittites regularly offered them to the gods.<sup>32</sup> In the near east, raisins were sometimes made by burying grapes in the desert sands. Viticulture soon spread to the Tigris-Euphrates region of North Africa, where raisins were made as early as the fourth millennium BC, owing to ideal environments and the already established tradition of drying fruits.<sup>33</sup> Grapes and raisins spread next to the Far East and the rest of North Africa, such as Morocco and Tunisia. The early Phoenicians and Egyptians, however, were eventually the ones to popularize the production and use of raisins and spread them throughout the western world, where they were valued for easy storage and transport.

In the European regions along the Mediterranean, the transition to increased production of raisins was particularly easy because of the preexisting tradition of viticulture and the existence of countless vineyards.<sup>29</sup> Sun drying had already become a custom there, making raisins and other preserved fruits easy to store and grind after harvest. Raisins were seen as a key source of nutrition that complemented the grains, beans, and cultured milks forming the foundation of the Mediterranean diet when Roman and Greek civilizations were at their peak. In fact, Ancient Greece and Rome represented the first major markets for raisins.<sup>34</sup> The cultivation of grapes in

Corinth in 500 BC later led to the naming of an early raisin variety as “currants,” deriving from “raisins of Corinth” and “black Corinth.”<sup>29</sup>

Ancient Romans ate raisins in spectacular quantities and all strata of society, included them as a major part of common meals, along with olives and bread. They picked the sweetest and plumpest grapes to dry, and featured them as a key part of the menu at Bacchanalian celebrations. Roman doctors also promoted the medicinal properties of raisins, prescribing them as a cure for a wide variety of ailments. Raisins were so valued that they transcended the food realm and became rewards for successful athletes as well as a premium barter currency. With the help of Roman legionnaires, vineyards and their products spanned the reaches of the empire, and remained a vital crop throughout Europe long after its fall.<sup>29</sup>

The history of raisins becomes a bit hazy until their reappearance in the 12<sup>th</sup> century AD. For the next 200 years of the Crusades, increased trade and movement between Europe and the East reinforced the popularity of the raisin, which was especially valued by traveling soldiers and adventurers.<sup>29</sup> This became especially important with the coming of the Age of Exploration. Spain in particular began to export raisins during the late 13<sup>th</sup> century. Soon afterwards, raisins became a popular luxury food in 14<sup>th</sup> century England. During the reign of Queen Elizabeth I, currants were used as a form of currency. Raisins later held an integral role in international markets as part of the "Triangular trade" in the 1700s between Europe, Africa and the Americas. Modern Europeans continued to value raisins as durable sources of energy and nutrients. In the two World Wars, raisins were seen as an ideal food for soldiers, and also helped to enliven “war cakes” and breads during times when eggs and sugar were in short supply.<sup>29</sup>

## **V. Raisins in California History**

California is today’s largest and most important sun-dried raisin provider, and has a history in raisin production originating with the state’s own colonization. In the early 1500s

missionaries sponsored by Queen Isabella established an important grape industry in Mexico near the American border. By the late 18<sup>th</sup> century, the missionaries had become experts at viticulture as well as the production of Muscat raisins. When they began to travel northward to build missions and settlements in California, missionaries such as Father Serra brought their agricultural techniques with them. The result was a tradition of grape and raisin production throughout California that was all the more ready to expand and develop when the US later developed a taste for the dried fruit.<sup>29 32 35</sup>

The California raisin industry in the San Joaquin Valley began to experience rapid growth in the 1870s and 1880s. In 1877, one of the first plantings was harvested in Fresno County (now the largest growing region in the US). The raisins were sold in San Francisco as an exotic food – quickly gaining popularity. The early agricultural centers for raisins were in Southern California and areas near Sacramento, but soon migrated to the warm, dry and fertile Fresno area. From there, raisins were sold and shipped throughout the US and later overseas. The industry grew rapidly due to the convenience of its location, as well as the fact that raisins were an alternative raw material for wine when fresh grapes were unavailable. During Prohibition, the opposite occurred when wine grape farmers produced raisins from their otherwise unusable crops. While the Muscat grape started as the predominant raisin grape variety, the Thompson Seedless soon became the preferred variety due to its seedless attributes.<sup>36</sup>

## VI. Raisin Production

Most of today's raisins – approximately 95% – are dried 'Thompson Seedless' grapes, *Vitis vinifera* L. This variety is followed by the 'Fiesta' (3%), and the 'Zante Currant' (1.5%). The term 'currant' is used to describe its small berry size, but it is a true grape and not a member of the *Ribes* species.<sup>37</sup> The terms "sultanas" and "raisins" are used inconsistently and sometimes interchangeably, from country to country. Outside the US, some make a distinction between these terms, generally using the former to refer to the naturally sun-dried Californian product and the latter to raisins that have been dried after treatment in various dipping solutions.

There are two methods for drying grapes to produce raisins. One involves natural sun drying for a period of 2 to 3 weeks, either in trays on the ground between the vines or hanging on the vines themselves. Another involves a short (15 to 20 seconds) exposure to hot water (87 to 93°C) and then placement in a dehydration tunnel (71°C) for 20 to 24 hours.

Raisins acquire their dark brown coloring from an accumulation of brown-black melanin pigments produced by polyphenol oxidase activity and non-enzymatic reactions. Golden raisins are Thompson Seedless grapes that have been dipped in hot water and treated with sulfur dioxide to prevent these darkening reactions.

Today, worldwide production of raisins and sultanas alone exceeds 1 million tons. Dried fruit is produced in most geographic regions of the world, and consumption occurs in all cultures and demographic segments. The US is the world's leading raisin producer. California accounts for over 90% of the total US grape production, using almost 3 million tons of grapes to produce approximately 400,000 tons of raisins per year.<sup>37</sup>

## VII. Nutrient Composition:

### i. Carbohydrates, vitamins and minerals

*Raisins, like most fruits, possess a combination of an appealing, sweet taste and nutritional value. Raisins provide essential nutrients, soluble and insoluble fiber, and health protective bioactive components, or phytochemicals.* Table 1 shows selected nutrient compositions of raisins and of Thompson Seedless grapes as a reference.<sup>38</sup> *Both raisins and grapes provide similar amounts of sugar (19.6g and 21.4g, respectively), divided almost equally between fructose and glucose with minimal amounts of sucrose. Raisins, like all fruits, are high in potassium and low in sodium. Compared to other fruits, they are high in magnesium and iron.*

Table 1. Selected Essential Nutrients in Grapes and Seedless Raisins<sup>38 i</sup>

| Nutrient       | Units | Values per Serving Seedless Raisins (32.5g) | Values per Serving Thompson Seedless Grapes (135g) |
|----------------|-------|---|--|
| Water          | g     | 5   | 108.6  |
| Energy         | kcal  | 97.5  | 93   |
| Carbohydrate   | g     | 25.7  | 24.6   |
| Sugars (total) | g     | 19.6  | 21.4   |
| Glucose        | g     | 9   | 9.8  |
| Fructose       | g     | 9.7   | 10.9   |
| Sucrose        | g     | 0.14  | 0.2  |
| Iron           | mg    | 0.6   | 0.48   |
| Magnesium      | mg    | 10.6  | 9.6  |
| Potassium      | mg    | 243   | 258  |

## ii. Boron

*Raisins are among the 50 major food contributors of boron in the American diet, having the highest concentration of boron at 2.2mg per 100g.<sup>39</sup> Boron, a putative essential trace element<sup>40</sup> is crucial for the growth and maintenance of healthy bones and joints.<sup>40 41</sup>*

<sup>i</sup> The serving sizes used in Table 1 reflect a 4.15 to 1.00 dry away ratio commonly observed when Thompson Seedless grapes are dried into raisins.

Controlled animal studies have shown that boron is essential for normal growth of both bone and cartilage and appears to have a role in the maturation of the bone growth plate.<sup>42</sup> Boron supplementation in rats and chicks has been shown to increase bone strength.<sup>43</sup> Boron deprivation, on the other hand, affects the skeletal system, the effect being most evident when the animals are simultaneously exposed to a nutritional stress, such as a deficiency in vitamin D, calcium, magnesium or potassium. Boron thus appears to positively affect vitamin D, calcium and magnesium metabolism. Boron deficiency has been reported in studies of rats and chickens and in three human clinical studies.<sup>44</sup>

***Boron may also have a preventive or therapeutic effect on osteoporosis by reducing bone calcium loss in postmenopausal women.*** Controlled boron deprivation studies indicate that boron has an essential role in maintaining bone density. In clinical studies including both men and women, boron supplementation after consumption of a low-boron diet increased previously suppressed 25-hydroxycholecalciferol (vitamin D) levels. Supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induced changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization.<sup>45</sup> In one study, estrogen therapy increased serum 17-beta-estradiol in postmenopausal women but not if they were fed low-boron diets. Although a mechanism that explains how boron affects bone formation and remodeling has yet to be defined, it appears that dietary boron may be required to convert estrogen and vitamin D to their more active form (17-beta-estradiol and 1,25-OH<sub>2</sub>D<sub>3</sub>, respectively). Recent animal studies support this hypothesis as results indicate that boron works synergistically with estrogen to exert its beneficial role on calcium and magnesium homeostasis. Investigators believe that ***boron may be an important nutritional factor determining the incidence of osteoporosis.***

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<sup>†</sup> Two expert scientific committees have reviewed literature on the significance of boron in human nutrition. A World Health Organization Expert Committee on *Trace Elements*. In: *Human Nutrition* has concluded that boron is “probably essential.” Additionally, a workshop on recommended intakes for trace elements sponsored by the USDA proposed that a provisional Recommended Dietary Allowance should be established for the mineral.

***Boron may also play a role in preventing arthritis.***<sup>46</sup> People suffering from osteoarthritis have been shown to have lower boron concentrations in femur heads, bones and synovial fluid than those without the disorder. In areas of the world where boron intake is usually 1 mg or less per day, the estimated incidence of arthritis ranges from 20 to 70%, whereas in areas where boron intake is usually 3 to 10mg, the estimated incidence of arthritis ranges from 0 to 10%. In Australia, where much of the produce is grown in boron-deficient soil, there is a high occurrence of osteoarthritis, and boron supplements have been widely considered an effective treatment.<sup>47</sup> Experimental evidence suggests that boron is also involved in the inflammatory process, or immune function. When an antigen was injected in rats to induce arthritis, those given boron supplements exhibited less swelling of the paws and lower circulating neutrophil concentrations than did those deficient in boron.<sup>48</sup>

***In conclusion, raisins are rich in boron, a mineral that is important for bone growth and maintenance. Boron in raisins may protect against osteoporosis by preventing bone loss and may have a role in preventing arthritis.***

### iii. Fiber

***High fiber diets have been promoted to help reduce the risk of developing various conditions, including constipation, heart disease, diabetes, diverticular disease, colon cancer and obesity. The Institute of Medicine and the Dietary Guidelines for Americans 2005 recommends that children (ages 1 and up) and adults consume 14g of fiber for every 1,000 calories of food they eat each day.***<sup>49 50</sup> ***However, most Americans consume far less fiber than the recommended amount. Dietary fiber intake among adults in the US averages about 15g. Raisins are a good source of soluble and insoluble fiber and help meet dietary fiber recommendations.***

The total dietary fiber content of raisins is 3.7g/100g, according to the USDA Nutrient Database.<sup>38</sup> However, ***other investigators have reported higher fiber levels for sun-dried, dipped and golden raisins: 5.05g/100g, 5.37g/100g and 5.05g/100g, respectively (Table 2).***<sup>51</sup> Soluble fiber accounts for about 30% of total fiber, golden raisins having slightly higher values.

Mannose is the predominant sugar in the soluble fiber. Insoluble fiber contains slightly more glucose than mannose residues. Pectin (measured as uronic acids) accounts for over 50% of total fiber. Lignin levels are low in all types of raisins.

**Table 2. Raisin Dietary Fiber Composition (grams per 100g)<sup>a 51</sup>**

| Raisin type | Soluble fiber |                         |       | Insoluble fiber |            |        |       | total fiber |
|-------------|---------------|-------------------------|-------|-----------------|------------|--------|-------|-------------|
|             | uronic acids  | Neutral PS <sup>b</sup> | total | uronic acids    | Neutral PS | lignin | total |             |
| Sun-dried   | 0.74          | 0.68                    | 1.42  | 2.06            | 1.56       | 0.01   | 3.63  | 5.05        |
| Golden      | 0.88          | 0.64                    | 1.52  | 2.23            | 1.61       | 0.01   | 3.85  | 5.37        |
| Dipped      | 1.07          | 0.69                    | 1.76  | 1.67            | 1.62       | nd     | 3.29  | 5.05        |

<sup>a</sup> Average of 3 determinations, AACC method 32-25

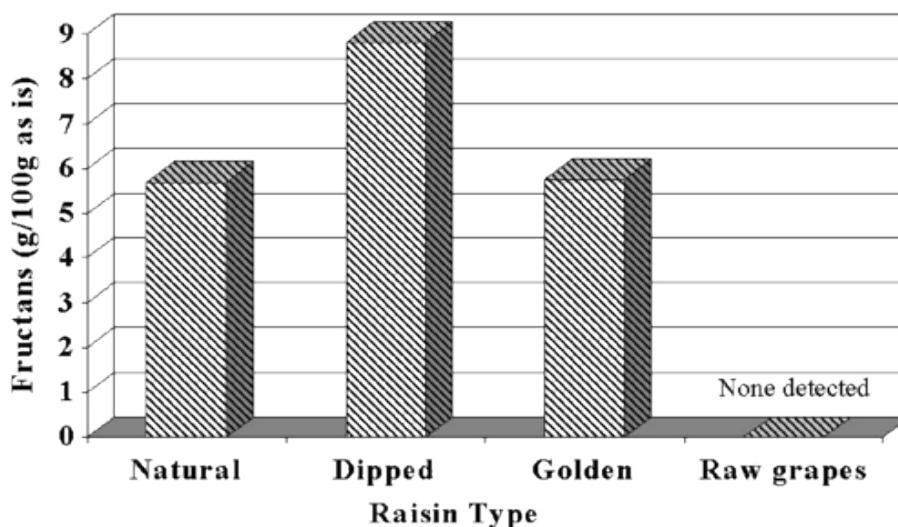
<sup>b</sup> Polysaccharide residues

***It is important to be aware that raisins provide over 5g of fructans per 100g (Figure 1).***

Fructans, also known as fructooligosaccharides (FOS), are fructosyl units bound by a beta (2-1)-glycosidic linkage. They are formed from the sugars in the grapes during the dehydration process. Fresh grapes themselves have no detectable fructans.<sup>51</sup> Both the American Association of Cereal Chemists and the Food and Nutrition Board definitions include fructans as components of dietary fiber. Yet, compounds in this group, which includes inulin, are soluble in aqueous ethanol and thus are not recovered in the Association of Official Analytical Chemists dietary fiber methods. ***Adding fructans to total fiber values of raisins nearly doubles their fiber content, suggesting that raisins can provide more fiber in the diet than was previously believed.***

.....

**Figure 1. Fructan Content of Raisins and Grapes<sup>51</sup>**



Studies have reported that dietary patterns, lifestyle exposure patterns, physical inactivity and obesity all increase colorectal cancer risk, especially in genetically predisposed populations. One element in the diet that has been strongly associated with protection from colorectal cancer is fiber.<sup>52 53 54</sup> The mechanisms for the beneficial effect of fiber in humans are still being elucidated and seem to be manifold. The presence of fiber in the diet decreases stool transit time, and so may hasten the elimination of carcinogens.<sup>55</sup> The addition of 120g of raisins (3 servings) to a daily diet shortened transit time by 14 hours.<sup>56</sup> Another mechanism involves the fermentation of fiber by colonic bacteria to produce short-chain fatty acids (SCFA). These acids are beneficial substrates for colonic epithelial cells and have a positive impact on the cells' resilience. *In vitro* studies using colon cancer cell lines have shown that butyrate may be potentially chemoprotective by inhibiting cell proliferation, stimulating cell differentiation, and inducing apoptosis.<sup>57 58</sup> Fibers that promote a butyrate-producing colonic ecosystem would thus have a protective effect against the developing of colorectal cancer. A study by Beyer-Sehlmeyer *et al*<sup>59</sup> showed that the effects of butyrate are enhanced *in vivo* by the mixture of products derived from the fermentation of fibers in the colon.

The increased concentration of acids in the colon would also inhibit the conversion of primary bile salts (cholic acid and chenodeoxycholic acid) to secondary bile acids (deoxycholic and lithocholic acids). A number of studies have shown that colorectal cancer patients have a higher level of secondary bile acids both entering and leaving the colon. Inclusion of raisins in the diet reduced the ratio of secondary to primary bile acid salts in the stools.<sup>60</sup> Thus, the acidic environment might be protective against the development of colon cancer. A recent article by Bell reviews the role of raisins in increasing total dietary fiber and the potential health benefits associated with consuming adequate fiber.<sup>61</sup>

*In conclusion, raisins are a high fiber food. Even a single serving of raisins provides a significant amount of fiber in a daily diet and can have beneficial effects on colon health. Adding fiber from high fiber foods such as raisins is preferable to using isolated fiber supplements because raisins deliver additional nutrients and phytochemicals that may also help to lower disease risks in other ways.*

## **VIII. Phytochemicals and Other Raisin Components of Physiologic Interest:**

### **i. Prebiotics, Raisins and Health**

*Raisins, unlike grapes, are a significant source of prebiotic compounds in the American diet.* An important effect of increasing fiber in the diet is its impact on the intestinal microflora. The growth of bacteria in the colon depends on the substrates that are available to them, i.e. compounds that have not been digested in the small intestine. *A prebiotic has been recently defined as “a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.”*<sup>62</sup> *Sun-dried raisins contain 5.7g fructans per 100g of fruit,<sup>51</sup> higher than all commonly consumed fruits.*<sup>63</sup> Fructans escape digestion in the upper g.i. tract and reach the large intestine practically intact. Here they are fermented by bacteria that can cleave the beta (2-1)-glycosidic

bonds between fructosyl units and act as prebiotic compounds by selectively stimulating the growth of beneficial intestinal microflora, namely bifidobacteria and lactobacilli. Clinical studies have shown that when taken in the diet, even at relatively low levels (5-20g/day), fructans increase manifold the numbers of these bacteria in the colon mucosa.<sup>64</sup>

A balanced microbiota in the intestinal track is essential for health and well-being. Prebiotics, such as fructans, help keep this balance by selectively stimulating the growth of health-promoting bacteria. The products of colonic fructan fermentation are lactic acid and short-chain fatty acids (SCFA), mainly acetate, propionate and butyrate, which play a significant role not only in colonic health but also the well being of the entire organism. ***The production and presence of SCFA and lactate in the colon alter the surroundings, creating a bacteriocidal environment for enteropathogens such as Escherichia coli and Clostridium perfringes. Including 120g of sun-dried raisins for 9 weeks in the diet of healthy adults increased total SCFA excretion.***<sup>60</sup>

***Prebiotics in raisins may play a role in colorectal cancer protection.*** Research using experimental animal models indicates that fructans have anticarcinogenic properties. For example, in rats, dietary fructans inhibit the formation of chemically-induced aberrant crypt foci. These are neoplastic lesions in the colon from which adenomas and carcinoma may develop.<sup>65 66 67</sup> The growth of bifidobacteria, have been shown to modify ras oncogene activity. Ras-gene activation is one of the earliest and most frequent genetic alterations associated with human cancers, specifically with colon cancer. Elevated levels of ras-p21 (the ras gene product) have been correlated with increased cell proliferation. Studies in rats have shown that ***Bifidobacteria longum*** can significantly suppress the expression of ras-p21 in the colonic mucosa and reduce tumor incidence.<sup>67</sup> In studies using human cell lines, fructan fermentation products have been shown to inhibit tumor cell growth, modulate differentiation and reduce metastatic activities.<sup>59</sup>

***Prebiotics in raisins may offer cardiovascular benefits through a triglyceride- and cholesterol-lowering effect.*** A recent meta-analysis of 16 clinical studies<sup>68</sup> showed that dietary

fructans significantly reduce serum triglycerides. The mechanism for this effect is still not clear, but it appears that fructans, like other soluble dietary fibers, reduce the capacity of hepatocytes to synthesize triglycerides from palmitate<sup>69</sup> and so lower net hepatic triglyceride synthesis. Given that fructans are not absorbed, how this effect is mediated is still a matter of speculation. One possible mechanism involves its fermentation products: an increased production of SCFA in the large intestine, particularly of propionic acid. This fatty acid has been shown to inhibit lipogenesis in isolated hepatocytes.<sup>70</sup> Other mechanisms involve modification of intestinal synthesis of cytokines and incretins, which enhance postprandial insulin secretion and so affect hepatic lipogenesis.

Studies on the cholesterol-lowering effect of fructans are not consistent, but encouraging results have been observed among hyperlipidemic subjects. Fructans, like fiber, may bind bile acids and increase their excretion in the feces. A continual depletion of bile in this manner may lower serum cholesterol levels by diverting cholesterol for bile acid synthesis. It is also possible that propionic acid, which increases with fructan colonic fermentation, inhibits hepatic cholesterol synthesis.<sup>70</sup>

***Prebiotics in raisins may stimulate calcium and magnesium absorption and so increase bone mineral content, bone density and maintain bone structure.*** Both animal and human studies have shown that non-digestible oligosaccharides can enhance mineral absorption, calcium retention and bone mineralization. In humans, the most convincing data comes from studies in young adolescents<sup>71</sup> and postmenopausal women.<sup>72</sup> The proposed mechanisms are manifold and include: increased solubility of minerals due to higher levels of SCFA generated by intestinal bacteria; increased surface area for mineral absorption via enhanced proliferation of enterocytes by fermentation products (lactate and butyrate); and increased expression of calcium-binding proteins in the large intestine.<sup>73 74 75</sup> Other methods by which fructans may increase mineral absorption include: modulating expression of bone-relevant cytokines; degradation of mineral-complexing phytic acid; increasing bioavailability of bone-modulating

factors such as phytoestrogens from foods; and improving overall intestinal health. These hypotheses have the experimental support of animal studies and continue to evolve.<sup>74</sup>

***In conclusion, fructooligosaccharides (fructans), formed from grape sugars during dehydration, give raisins a unique set of health benefits. Not only do they increase dietary fiber content and help regulate bowel functions, but acting as prebiotic agents, they stimulate health-promoting intestinal flora, maintain intestinal balance, may contribute to cardiovascular health, may protect from colon cancer, may increase absorption of calcium and magnesium and so enhance bone mineralization during growth and protect from osteoporosis after menopause. Humans have shown beneficial effects of fructans at doses as low as 7g per day. A single serving of raisins provides about a third of this amount.***

## ii. Tartaric Acid

***Sun-dried raisins have beneficial effects on colonic function that go beyond those due to their fiber content alone.*** Grapes and raisins are the only fruits that contain significant levels of tartaric acid (TA) in temperate regions of the world. Because of its low solubility in water, some of the TA in grapes is lost during processing of grape juice and wine, and so ***grapes and raisins remain the most practical sources of tartaric acid in the American diet.*** Grapes contain 0.6-0.9g/100g of TA and raisins contain 2.0-3.5g/100g of TA.<sup>56</sup> Studies on tartaric acid have shown that its presence in the diet has a positive impact on colonic health. A study comparing the effect of a low-fiber, grape-free diet to one containing either 120g of sun-dried raisins or 5g cream of tartar (approximately equivalent to the amount of TA in the raisins) on intestinal function in healthy adults found that both diets shortened intestinal transit time.<sup>56</sup> The effect was greater among those in the raisin diet. Because of the higher fiber content of this diet, fecal bulk and fecal moisture content also increased. In a second study by the same investigators, participants consumed diets containing 84g, 126g or 168g of sun-dried raisins daily.<sup>56</sup> Transit time decreased and fecal weight increased with increasing content of raisins in the diet. Both studies found that sun-dried raisins and TA lowered total fecal bile acid concentration, mainly due to a reduction in lithocholic and deoxycholic acid. All these parameters of intestinal function may

play a role in the prevention of colon cancer. A shortened transit time may hasten the elimination of carcinogens, toxic compounds and byproducts of metabolism and an increased fecal weight may result in dilution of fecal carcinogens – either endogenous or exogenous. Fecal bile concentration has been directly associated with colon cancer risk, both lithocholic and deoxycholic acid acting as co-mutagenic compounds in a variety of *in vitro* assays. The results of these studies suggest ***that tartaric acid and fiber in raisins work synergistically to maintain a healthy digestive system. They also make a strong case for the advantages of combining foods with beneficial effects, such as raisins with high cereal fiber foods.***

Tartaric acid has also been shown to help increase the bioavailability of minerals in the diet, such as calcium and iron. *In vitro* studies indicate that tartaric acid increases the uptake of iron by Caco-2 cells by lowering intestinal pH and by forming soluble iron-acid complexes, especially with ferric ion.<sup>76 77</sup> Studies using *in vitro* simulated gastrointestinal digestion showed that tartaric acid increases the calcium availability from vegetables.<sup>78</sup> Investigators trying to find a way to reduce the rates of anemia in India developed an iron-fortified biscuit and tested iron bioavailability with and without tartaric acid. They found that by adding tartaric acid, they were able to increase iron availability by 338%.<sup>79</sup> ***Tartaric acid content of grapes and raisins make a strong case for adding these fruits to foods where minerals are poorly absorbed. Raisins paired with iron-fortified cereals will enhance iron absorption; raisins in vegetable salads may not only add zest but may enhance calcium absorption.***

Unlike other fruit acids (such as malic and citric acid), tartaric acid bypasses the small intestine and is fermented by colonic bacteria to produce short-chain fatty acids (SCFA). As discussed in the previous section, these acids play a significant role not only in colonic health but also in the well being of the entire organism. ***Tartaric acid may act synergistically with fructans to enhance the potential of raisins as a prebiotic food.***



### iii. Polyphenols in Sun-Dried Raisins

*Raisins are an excellent source of polyphenols in the American diet. Polyphenols make up the largest group of phytochemicals in the diet and they appear to be, at least in part, responsible for the potential health benefit associated with the consumption of diets abundant in fruits and vegetables.*

Polyphenols are synthesized by all vascular plants and are therefore present in all plant foods contributing to their color and taste. Polyphenols have many functions essential to plant growth and survival. In animals and humans who consume them, they affect cellular biochemistry. They are potent antioxidants and may protect cell constituents against oxidative damage. They chelate metals, modulate enzymatic activity, inhibit cellular proliferation and alter signal transduction pathways. Current evidence strongly supports a role for polyphenols in the prevention of cardiovascular disease, cancer and osteoporosis and suggests a role in the prevention of neurodegenerative diseases, diabetes and inflammatory disorders.

Total polyphenol content can be estimated from absorbance measures at 280 nm or by using specific agents such as Folin Ciocalteu.<sup>†</sup> Using this assay, raisins, figs and prunes show similar total phenolic content ranging from about 9mg to 12mg of gallic acid equivalents per gram of fruit (Table 3).<sup>80</sup> Values are higher for dried fruit than the corresponding values for fresh fruit because the phenols are concentrated during the dehydration process. However, total phenolic values are still higher when expressed on a per serving basis (from NLEA defined serving size).<sup>38</sup> For a comprehensive review on raisin polyphenols see Williamson *et al.*<sup>81</sup>

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<sup>†</sup> This assay is based on an oxidation reaction. Although it is used to compare samples with similar composition, it is imprecise in assays of extracts of different polyphenol structures.

**Table 3. Total Phenolics of Dried Fruits and Grapes<sup>80 a</sup>**

| Food               | Total Phenolics <sup>b</sup><br>(mg of AE/g) | Serving Size<br>NLEA (grams) | Total Phenolics<br>Per Serving<br>(mg of GAE) |
|--------------------|--|------------------------------|---|
| Dates: Deglet Noor | 6.61 ± 1.11                                  | 40                           | 264   |
| Dates: Medjool     | 5.72   | 40                           | 228   |
| Figs               | 9.60 ± 0.07                                  | 40                           | 384   |
| Prunes             | 11.95 ± 1.56                                 | 40                           | 478   |
| Raisins            | 10.65 ± 1.59                                 | 43                           | 458   |
| Green Grapes       | 1.45 ± 0.11                                  | 126                          | 183   |

<sup>a</sup> Data presented as mean ± SD for sample numbers, expressed on a “as consumed” weight basis. <sup>b</sup> Total phenolics data expressed as milligrams of gallic acid equivalents per gram (mg of GAE/g).

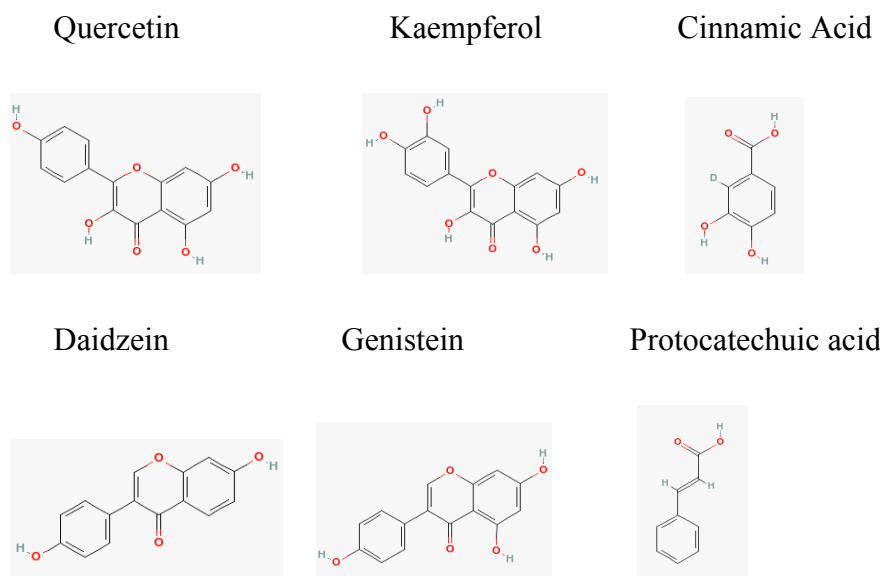
Plant polyphenols are very diverse and have complex chemical structures. They can be classified into flavonoids and phenolic acids. There are several subclasses of flavonoids in foods. *In raisins, the most abundant are the flavonols quercetin and kaempferol. Raisins are unique among fruits and nuts in their relatively high content of the isoflavones daidzein and genistein. In addition, raisins are rich in the phenolic acids caftaric and coutaric acid.*<sup>†</sup>

Figure 2 shows the structure of selected polyphenols in raisins.

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<sup>†</sup> Caftaric and coutaric acids are the tartaric acid esters of hydroxycinnamic acids p-coumaric acid and caffeic acid.

**Figure 2. Selected Polyphenols and Phenolic Acids Found in Raisins**



While the phenolic composition of grapes, grape juices and wines have been investigated by many researchers, there are only two reports in print on the polyphenol composition of raisins (Karadeniz *et al*<sup>82</sup> Parker *et al*<sup>83</sup>) in addition to the USDA Database for the Flavonoid Content of Selected Foods.<sup>84</sup> Raisin polyphenolic profile is strikingly different from that of Thompson Seedless grapes (Tables 4, 5 and 6). This is due to both enzymatic oxidation and non-enzymatic browning reactions that happen during dehydration of grapes. Both reports show similar trends: the concentration of quercetin glycosides are the highest among flavonols followed by that of kaempferol glycosides. The content of rutin is relatively low among the flavonols determined and was detected only in raisins by Parker *et al*.<sup>83</sup> On the other hand oxidized cinnamics and protocatechuic acid were only detected in sun-dried<sup>83</sup> and dipped raisins.<sup>82</sup> Golden raisins contained the highest amount of *trans*-caftaric and *trans*-coutaric acids.<sup>82</sup> Sulfur dioxide curtails oxidation in these raisins resulting in a higher phenolic content. When compared to fresh grapes, Karadeniz reported a loss in phenolic acids of up to 90% and a loss of flavonols in the order of 60%.<sup>82</sup> This is not consistent with Parker's report, who reports lower losses. According to Karadeniz, procyanidins and flavanols are completely degraded during raisin formation.<sup>82</sup> This is also inconsistent with the USDA database which lists raisin catechins content of

0.42mg/100g, epicatechins at 0.10mg/100g and cianidin at 0.03mg/100g of fruit.<sup>84</sup>

Unfortunately, the original report from which these results are based is not yet in print.<sup>85</sup>

Finally, Karadeniz detected no resveratrol or ellagic acid in fresh grapes or raisins.<sup>82</sup> While the many changes that grape polyphenols undergo during their conversion into raisins is out of the scope of this paper, one should be aware that they yield highly complex structures, many flavonoids (e.g. flavanols) condensing into large molecules or polymers (tannins). The difficulty in working with the raisin matrix and interference with non-phenolic compounds may explain the difference in the reported values.

**Table 4. Phenolic Acid Compositions of Raisins and Grapes\* <sup>82</sup>**

| Sample                           | Oxidized Cinnamics |     | Caftaric acid |       | Coutaric acid |       | 2-S-glutathionyl caftaric acid | Protocatechuic acid |
|----------------------------------|--------------------|-----|---------------|-------|---------------|-------|--------------------------------|---------------------|
|                                  | A                  | B   | cis           | trans | cis           | trans |                                |                     |
| Sun-dried raisins (n = 10), mean | 3.7                | 6.1 | nd            | 39.6  | nd            | 6.7   | nd                             | 6.8                 |
| Dipped raisins (n = 5), mean     | 2.9                | 5.1 | nd            | 45.2  | nd            | 7.7   | 8.1                            | 2.8                 |
| Golden raisins (n = 5), mean     | nd                 | nd  | nd            | 84.3  | nd            | 27.3  | nd                             | nd                  |
| Fresh grapes                     | nd                 | nd  | 2.7           | 100.7 | 8.0           | 31.8  | nd                             | nd                  |

\* mg/kg of sample

**Table 5. Flavonol Glycoside Composition of Raisins and Grapes\* <sup>82</sup>**

| Sample                           | Rutin | Quercetin glycoside |      | Kaempferol glycoside |      |
|----------------------------------|-------|---------------------|------|----------------------|------|
|                                  |       | A                   | B    | A                    | B    |
| Sun-dried raisins (n = 10), mean | 5.2   | 7.3                 | 34.7 | 11.2                 | 23.7 |
| Dipped raisins (n = 5), mean     | 6.5   | 20.6                | 39.0 | 16.7                 | 29.5 |
| Golden raisins (n = 5), mean     | 3.5   | 41.5                | 37.1 | 6.5                  | 7.6  |
| Fresh grapes                     | 0.9   | 21.9                | 3.9  | nd                   | 19.4 |

nd = not detected      \* mg/kg of sample

**Table 6. Flavonoid, and Phenolic Composition of Grapes and Raisins** <sup>\* 83</sup>

|                                | Raisin            |                      | Grape            |                   |
|--------------------------------|-------------------|----------------------|------------------|-------------------|
|                                | golden<br>(n = 4) | sun-dried<br>(n = 3) | fresh<br>(n = 3) | frozen<br>(n = 3) |
| <i>trans</i> -caftaric acid    | 130.4 ± 7.0       | 41.4 ± 5.8           | 7.9 ± 1.5        | 7.9 ± 0.19        |
| <i>trans</i> -coutaric acid    | 34.1 ± 8.8        | nd                   | 14.8 ± 1.0       | nd                |
| 2-S-glutathionyl caftaric acid | Nd                | nd                   | 8.8 ± 0.9        | 12.1 ± 4.4        |
| protocatechuic acid            | Nd                | 4.4 ± 1.2            | Nd               | nd                |
| Rutin                          | 14.4 ± 0.9        | 8.3 ± 1.6            | trace            | trace             |
| quercetin glycoside A          | 65.7 ± 13.7       | 15.6 ± 2.8           | 15.2 ± 3.1       | 21.5 ± 4.7        |
| quercetin glycoside B          | 43.4 ± 5.2        | 6.5 ± 0.3            | 25.6 ± 3.7       | 27.7 ± 6.5        |
| kaempferol glycoside A         | 9.8 ± 0.5         | 7.0 ± 3.1            | trace            | trace             |
| kaempferol glycoside B         | 14.3 ± 2.9        | 9.3 ± 2.6            | trace            | trace             |

nd = not detected

\*mg/kg of sample ± SD

Daidzein and genistein are isoflavones with estrogenic activity in humans, and therefore are known as phytoestrogens. Structurally they resemble 17 $\beta$  estradiol and in *in vivo* assays they compete with the hormone at the receptor level. As other flavonoids, they may act as cellular antioxidants; they are potent tyrosine kinase inhibitors<sup>†</sup> and affect cell cycle. They have been shown to protect against breast, prostate and other cancers, lower risk of cardiovascular disease and alleviate menopausal symptoms.

<sup>†</sup> Tyrosine kinase activity leads to the activation of multiple cellular pathways involved in tumor growth, differentiation, transformation, proliferation, metastasis, and inhibition of apoptosis. The TK proteins comprise the largest family of oncogenes that are altered in many cancers.

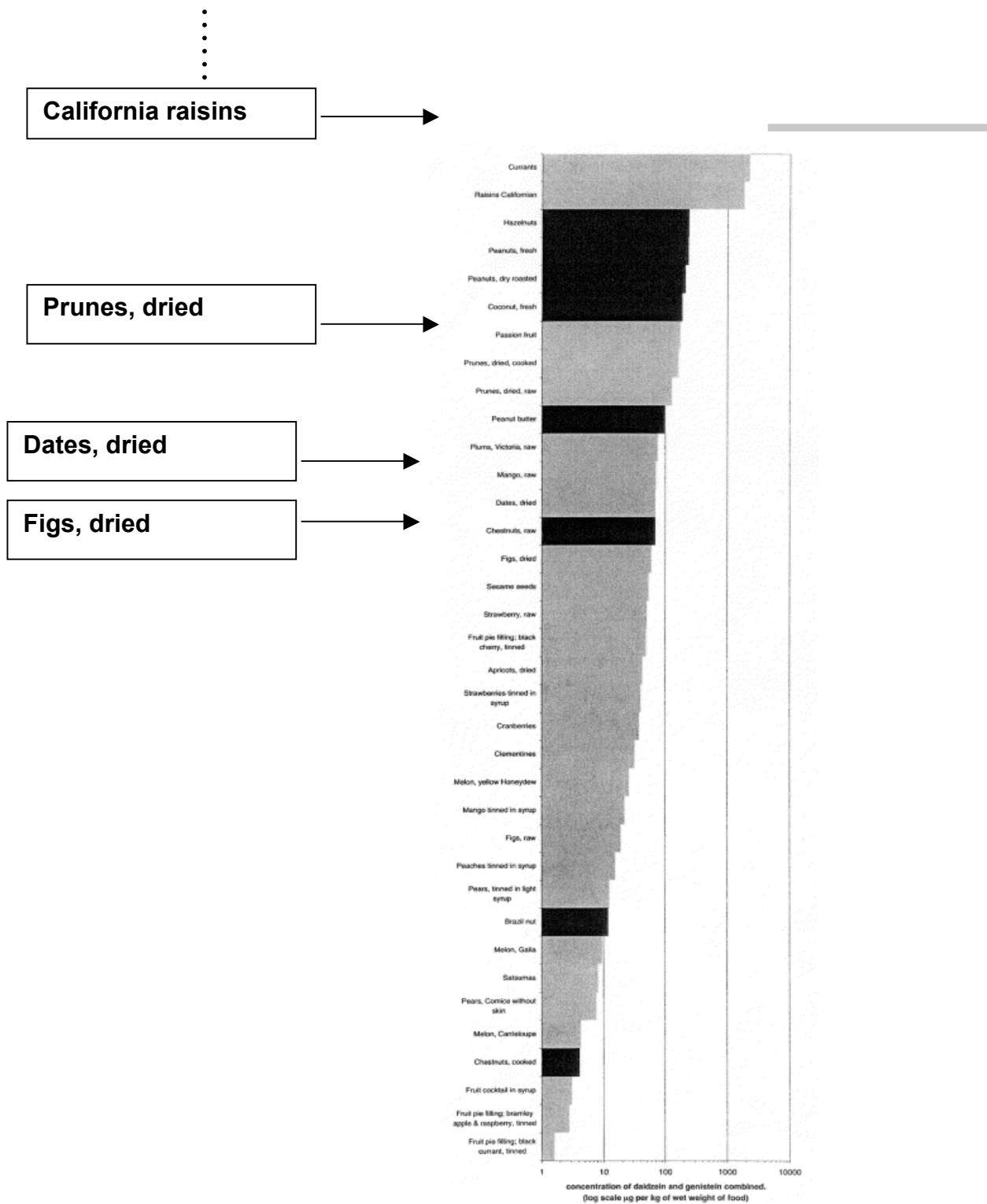


Figure 3. Comparison of the combined concentration of daidzein and genistein in different fruit (grey) and nuts (black)<sup>86</sup>

The concentrations of daidzein and genistein have been determined in a variety of fruits and nuts commonly eaten in Europe.<sup>86</sup> *Of the 36 samples of fruits and nuts that contain daidzein or genistein, currants and California raisins are the richest sources, containing 2.25 and 1.84mg/kg, respectively.* The other 34 foods contain between 0.250 and .001mg/kg wet weight of food (Figure 3). In comparison, soybeans contain approximately 2g/kg wet weight.<sup>87</sup> While even a small portion of a soy product in the diet adds very significant concentrations of daidzein and genistein, *inclusion of raisins in the diet will contribute to the daily intake of these protective phytochemicals.*

## IX. Health Effects

### i. Antioxidant Capacity of Sun-Dried Raisins

*By virtue of their high polyphenol content, raisins are an important source of antioxidants in the American diet. These phytochemicals are believed to account for a major portion of antioxidant capacity in plant foods. Antioxidants can lower oxidative stress and so prevent oxidative damage to critical cellular components.*

Current scientific thought regards oxidative stress as an important contributing factor in the development of heart disease and cancer, the two leading causes of death in the US. It is also implicated in the development of neuronal degeneration such as in Alzheimer's and Parkinson's disease as well as in the aging process itself.<sup>88</sup> Oxidative stress is an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense system and can result from either a deficiency in the antioxidant defense mechanism or from an increase in ROS levels. ROS is a collective term that includes oxygen and non-oxygen radicals and comprises superoxide, hydroxyl, peroxy, alkoxyl and nitric oxide derived products. They are generated as byproducts of normal cellular respiration that is essential to life and by the immune system and so contribute to our defenses. Higher levels can be generated from excessive activation of ROS

systems, such as those mediated by chronic inflammation and infection or by instances of increased oxygen uptake such as in strenuous exercise. Exposure to ROS-generating chemicals and environmental toxins (i.e. tobacco smoke, pollutants, food constituents, ethanol and radiation) contribute to the total burden. Organisms have developed a very delicate system to eliminate or neutralize ROS, but it is not 100% effective. In addition to endogenous antioxidant enzymes, they can be scavenged by antioxidants obtained from the diet. The term “antioxidant” has been defined by the Institute of Medicine of the National Academy of Sciences as “a substance in foods that significantly decreases the adverse effects of reactive species, such as reactive oxygen species, on normal physiological functions in humans.” Examples include phenolics, carotenoids and vitamins E and C found predominantly in plant foods.

Many *in vitro* methods have been used to compare the oxidation/reduction potential of foods and their phytochemicals. These include the oxygen radical absorbance capacity (ORAC), total radical-trapping antioxidant parameter (TRAP); Trolox equivalent antioxidant capacity (TEAC); and the ferric reducing/antioxidant power (FRAP). These assays are based on different mechanisms using different radical or oxidant sources and therefore generate different values and cannot be compared directly. In general, a food that has a high value for one measure of antioxidant capacity will also be high for another measure. The ORAC assay is considered by some to be a preferable method because of its biological relevance to the *in vivo* antioxidant efficacy.<sup>89</sup> Researchers at the USDA have measured both lipophilic (L-ORAC) and hydrophilic (H-ORAC) antioxidant capacities of common foods in the US using the ORAC assay. They have calculated total antioxidant capacity (TAC) by combining L-ORAC and H-ORAC, and a database is available.<sup>80</sup> Most recently, the cellular antioxidant activity assay (CAAA) has been developed to measure antioxidant activity in cell culture. It is a more biologically relevant assessment because it takes into account some aspects of antioxidant cellular uptake, metabolism and location within cells.<sup>90</sup>

Values for antioxidant capacity of raisins and/or grapes assessed by different methods are listed in Table 7. ***TAC per 100g of fruit in sun-dried raisins is higher than in fresh Thompson***

***Seedless and red grapes due to the concentration of antioxidants during dehydration (3037, 1118 and 1260  $\mu\text{mol}/100\text{g}$  of fruit).***<sup>80</sup> This is consistent in all dried fruits. Other than the phenolic compounds, several components of raisins and dried fruits can contribute to their antioxidant potential such as organic acids and Maillard Reaction products. However, this has not yet been investigated. It is interesting to note that the ORAC for golden raisins is much higher per gram than the value for sun-dried raisins (10,480 versus 3,740  $\mu\text{mol}/100\text{g}$ , respectively).<sup>83</sup> Golden raisins are treated with hot water and  $\text{SO}_2$  to inactivate polyphenol oxidase and to inhibit nonenzymatic browning, probably allowing the raisin to retain the phenolic antioxidants of the original grape, which are then concentrated during drying. Total antioxidant activity in dried fruits, much like in all fruits, parallels their phenolic content.

Fruits are among the major antioxidant sources in our diet. Grapes and raisins on a per serving basis have intermediate to high values of TAC among fruits commonly consumed in the US, lower than berries and plums and higher than all melons, bananas, peaches, nectarines, apricots and many citrus fruits. ***When fruits and vegetables are categorized into groups ranked by their H-ORAC expressed on a per serving basis, raisins are grouped within the highest quartile (Table 8).***<sup>80</sup> ***Because H-ORAC makes up most of the TAC, the foods in this group can be regarded as the best source of total antioxidant capacity.*** Lipophilic values are very low in most fruits and vegetables compared to hydrophilic ones, which make up  $\geq 90\%$  of TAC. ***The contribution of L-ORAC to TAC is similar in fresh and dried fruits indicating that the drying process does not change the proportion of hydrophilic and lipophilic ORAC.***<sup>80</sup>

**Table 7. Antioxidant Capacity of Raisins and Grapes Reported in the Literature**

| Method/Investigator   | Sun-Dried Raisins | Golden Raisins | Thompson Seedless Grapes | Red Grapes |
|---|-------------------|----------------|--------------------------|------------|
| ORAC (μmol TE/100 g fruit ±SD) Parker, 2007 <sup>83</sup>                     | 3740 ± 370        | 10480 ± 870    | 1080 ± 490               | -          |
| Cellular Antioxidant Activity (μmol QE/100 g fruit) Wolfe, 2007 <sup>90</sup> | -                 | -              | 939 ± 48                 | 2410       |
| Lipophilic ORAC (μmol TE/100g) Wu, 2004 <sup>80</sup>                         | 35 ± 13           | -              | NA                       | NA         |
| Hydrophilic ORAC (μmol TE/100g) Wu, 2004 <sup>80</sup>                        | 3002 ± 523        | -              | 1118 ± 166               | 1260 ± 317 |
| Total ORAC (μmol TE/100g) Wu, 2004 <sup>80</sup>                              | 3037              | -              | 1118                     | 1260       |
| FRAP (mmol Fe2+/kg) Pellegrini 2006 <sup>91</sup>                             | 23.26             | -              | -                        | -          |
| TRAP (mmol Trolox/kg) Pellegrini 2006 <sup>91</sup>                           | 6.7               | -              | -                        | -          |
| TEAC (mmol Trolox/kg) Pellegrini 2006 <sup>91</sup>                           | 6.63              | -              | -                        | -          |
| FRAP (mmol antioxidant content/100g) Halvorsen 2006 <sup>92</sup>             | 0.78              | -              | 0.133                    | 0.316      |

Data presented as mean  $\pm$  SD. ORAC<sub>FL</sub> data expressed as micromoles Trolox equivalents per gram (  $\mu$ mol of TE/g).

**Table 8. Common Foods Categorized into Four Groups Ranked by Their Hydrophilic ORAC<sub>FL</sub> (H-ORAC<sub>FL</sub>) per Serving<sup>a 80</sup>**

| H-ORAC <sub>FL</sub> <sup>b</sup><br>( $\mu$ mol of TE/serving) | Foods  |
|---|--|
| <b>14000-2000</b>   | bean, small red; blueberry, wild; bean, red kidney; bean, pinto; blueberry, cultivated; cranberry; artichoke (C); blackberry; prune; strawberry; raspberry; apple, Red Delicious and Granny Smith; pecan; cherry, sweet; plum, black; potato, russet; potato, russet (C); plum; bean, black; apple, Gala; walnut; apples, Golden Delicious and Fuji; date, Deglet Noor; pear, Green and Red Anjou cultivars; hazelnut; orange, navel; <b>raisin</b> ; fig; avocado, Haas; broccoli raab (R); cabbage, red (C); potato, red; potato, red (C); potato, white; pistachio; date, Medjool; bean, navy; grape, red |
| <b>1999-1000</b>  | asparagus; pea, blackeye; beet; grapefruit, red; potato, white (C); grape, green; pepper, yellow; peach; pepper, orange; mango; asparagus, (C); apricot; tangerine; cereal, low-fat granola with raisin (K); onion, yellow (C); broccoli raab (C); almond; pineapple; sweet potato, (C); cereal, squares toasted oatmeal (Q); lettuce, red leaf; sweet potato; radish; pepper, red; eggplant; cereal, toasted oatmeal (Q); cereal, oat bran (Q)  |
| <b>999-500</b>  | nectarine; banana; broccoli, (C); onion, red; spinach; cereal, oat bran hot (Q); peanut; onion, yellow; cabbage, red; cereal, oat, quick 1-min (Q); carrot; cereal, corn flakes Total (GM); kiwifruit; pepper, green; snack, fruit and oatmeal, strawberry (Q); broccoli; cereal, Original Shredded Wheat (P); pepper, red (C); cereal, instant oatmeal (Q); lettuce, green leaf; cereal, oats old fashioned (Q); bread, butternut all whole grain wheat; bread, pumpernickel (B); snack, oatmeal raisin cookie (PF); tomato, (C)  |
| <b>499-0</b>  | pumpkin; cantaloupe; onion, sweet; cabbage; bread, oatnut (B). corn; cereal, Life (Q); cashews; pepper, green (C); peach, canned; snack, chewy low-fat granola bar (Q); macadamia; pea, green and frozen; lettuce, butterhead; honeydew; tomato; corn, canned; corn, frozen; bread (HC); lettuce, romaine; celery; cauliflower; bean, lima and canned; pea, green and frozen; Brazil nut; carrot, baby; watermelon; carrot, (C); bean, snap and canned; popcorn, buttered, premium (PS); lettuce, iceberg; pine nuts; bean, snap and fresh; cucumber, peeled and with peel                                   |

<sup>a</sup> Foods are listed in order within each group from highest to lowest ORAC value per serving.



**Table 10. Antioxidant Activity of Dried Fruits as Measured by FRAP, TRAP and TEAC Assays<sup>a b 91</sup>**

| Dried Fruit | FRAP (mmol FE <sub>2</sub> <sup>+</sup> /kg) |      | TRAP (mmol Trolox/kg) |      | TEAC (mmol Trolox/kg) |      |
|-------------|--|------|-----------------------|------|-----------------------|------|
|             | Value  | Rank | Value                 | Rank | Value                 | Rank |
| Apricot     | 36.64  | 2    | 13.33                 | 2    | 12.87                 | 2    |
| Chestnut    | 20.63  | 4    | 12.85                 | 3    | 4.40                  | 5    |
| Fig         | 14.43  | 5    | 1.96                  | 5    | 5.02                  | 4    |
| Prune       | 60.54  | 1    | 23.00                 | 1    | 14.82                 | 1    |
| Raisin      | 23.26  | 3    | 6.17                  | 4    | 6.63                  | 3    |

<sup>a b</sup> Values are mean, n=3. Values represent the sum of water and lipid soluble extracts.

Antioxidant quality is a measure of the effectiveness of the antioxidant(s) present as a pure compound or a mixture. Investigators have estimated the quality of antioxidants in fruits and vegetables extracts by determining the IC<sub>50</sub> (the concentration to inhibit *in vitro* oxidation of LDL particles by 50%) of the pooled phenol extracts. Figure 4 compares antioxidant quality of dried fruits to that of antioxidant vitamins expressed as 1/IC<sub>50</sub>. The higher the value, the better the antioxidant quality. ***The antioxidant quality of phenols in the dried fruits is significantly higher than that of vitamins by nearly a factor of 10.*** These investigators have shown that phenolic antioxidant quality seems to improve during the drying process.<sup>94</sup> The 1/IC<sub>50</sub> values for fresh cranberries, green grapes and plums are 1.16, 1.32 and 1.42, respectively.<sup>95</sup> Those for



antioxidant activity increased as measured by the FRAP assay (but not the TRAP assay) after 2 and 4 weeks. In another study, 210g of sun-dried raisins homogenized in water (equivalent to 3570  $\mu\text{mol TE}$ ) were fed to 12 healthy adults.<sup>99</sup> Their plasma ORAC was measured at fasting (baseline) and 15, 30 and 60 minutes after drinking the raisin preparation. Blood ORAC levels were higher at the three testing times, reaching peak values at 30 minutes and declining after 60 minutes, while still remaining higher than baseline values. In the most recent study, healthy adults were fed 250g Thompson Seedless grapes, 50g of sun-dried raisins or 50g golden raisins for 4 weeks.<sup>83</sup> Serum ORAC was measured after a 12-hour fast and 1 and 2 hours after eating the test sample with a bagel and water. There was an apparent trend toward increasing serum antioxidant capacity by the second and third week of sample consumption, although values fell again in the fourth week (Figure 5). Authors speculated that there may be a physiological plateau approximately 2 or 3 weeks after consistent consumption. Participants however were free living and no restrictions were made on their diets during the study, so many explanations are possible. No consistent serum ORAC changes were seen 1 and 2 hours after grapes/raisins and bagel consumption. Other studies have shown that antioxidant rich foods are able to increase postprandial antioxidant capacity.<sup>100</sup> For example, feeding Sprite™ lowers plasma antioxidant capacity, but feeding Sprite™ plus dried figs raises plasma antioxidant capacity above baseline levels for up to 4 hours, overcoming the pro-oxidant effect of the sugar consumption.

A recent study<sup>101</sup> found that eating raisins daily raises serum ORAC in healthy but overweight individuals. ORAC measures the combined capacity of antioxidants, particularly water soluble ones, to lower levels of oxidants that may damage susceptible molecules. ORAC is thus influenced by blood levels of vitamin C, uric acid and flavonoids. In this study, 17 overweight men and women either ate 90g raisins or isocaloric placebos for 14 days in a randomized, cross-over design while following a low-flavonoid diet. After the raisin intervention, individuals had higher blood ORAC levels (Table 11). This suggests that the antioxidants in raisins, probably phenolic compounds and flavonoids, may raise the antioxidant

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defense capacity of blood either through direct scavenging or by modulating the activity of other antioxidants. It has been hypothesized that fruit consumption may also raise total blood antioxidant capacity because of the higher uric acid levels resulting from fructose metabolism.

While blood ORAC increased with the raisin intervention, urinary 8-epi PGF<sub>2α</sub> level, a measure of oxidative stress, did not change. This lack of consistency between measures of antioxidant capacity and markers of oxidative stress have previously been reported. Because of the complex relationship between the two, future studies that include a range of oxidative stress markers may be necessary to fully investigate the potential antioxidant effects of raisin consumption.

**Table 11. Fasting ORAC values before and after raisin and placebo intervention<sup>‡</sup>**

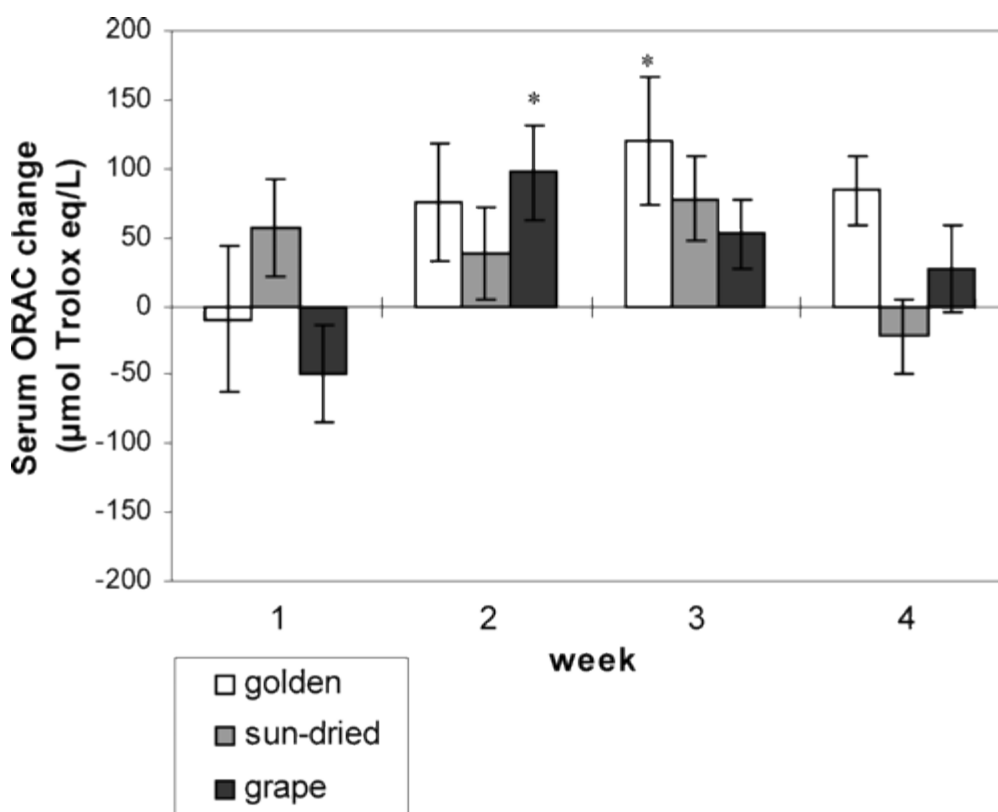
| Variable                                    | Pre-raisin          | Post-raisin         | Pre-placebo         | Post-placebo        |
|---|---------------------|---------------------|---------------------|---------------------|
| ORAC total (μmol/L TE)*,†                   | 7163<br>(6479–7919) | 7614<br>(6887–8417) | 8336<br>(7540–9215) | 8403<br>(7601–9290) |
| ORACpca (μmol/l TE)*,†                      | 886<br>(823–954)    | 932<br>(866–1004)   | 980<br>(910–1055)   | 1015<br>(94–1093)   |
| Urinary 8-epi PGF <sub>2α</sub> (pg/mg CR)* | 4164<br>(3538–4901) | 3108<br>(2641–3657) | 4298<br>(3665–5040) | 3485<br>(2972–4087) |
|   |                     |                     |                     |                     |

8-epi PGF<sub>2α</sub> = 8-epi-prostaglandin-F<sub>2</sub>; values are means with 95% CI.

\* Significant effect of pre/post when interventions combined.

†Significant difference for raisin and placebo treatment; ‡ Adapted from Rankin *et al*

**Figure 5. Long-term Serum ORAC (Oxygen Radical Absorbance Capacity) Change Over 4 Weeks of Daily Consumption of Golden Raisins, Sun-dried Raisins or Grapes<sup>83</sup>**



Note: Higher values indicate a higher serum antioxidant capacity. Baseline is zero. Baseline raw values: golden, 1113; sun-dried, 1155; and grape, 1095 μmol TE/L. \* $p < 0.05$ . Shown as means  $\pm$  SEM ( $n \geq 9$ ).

Investigators have looked at the effect of feeding different antioxidant vitamins and diets high in certain fruits and vegetables on levels of 8-hydroxy-2-deoxyguanosine (8OHdG) in the urine or in leukocytes.<sup>102 103</sup> 8OHdG is a product of free radical oxidative damage to DNA or to the DNA precursor pool. Studies looking at the effect of pure antioxidants such as the vitamins E and C, beta-carotene or coenzyme Q10 do not change 8OHdG,<sup>104</sup> whereas feeding polyphenol-rich fruits and vegetables such as wine, Brussels sprouts<sup>105</sup> and mixed diets high in

phenolics.<sup>106</sup> Intense physical activity increases oxygen uptake with a potential for increased formation of reactive oxygen species. These can cause damage to large biomolecules such as proteins and DNA if such an increase exceeds the protective capacity of the antioxidant defense mechanisms.<sup>107 108</sup> Oxidative stress therefore points to a risk of degenerative disease and premature aging from extreme exercise. ***Foods high in phenolic antioxidants can protect against DNA damage during intense physical activity by counteracting oxidative stress.*** Feeding 170g of sun-dried raisins prior to and during a triathlon to trained athletes significantly lowered 8OHdG urine levels compared to feeding of a glucose drink with the same amount of calories.<sup>109</sup> This suggests ***that during strenuous exercise, foods rich in phenolic antioxidants such as sun-dried raisins can protect from DNA damage due to oxidative stress.***

Another measure of oxidative stress is a measure of circulating oxidized LDL particles (ox-LDL). They can provide a measure of tissue damage and can be a useful marker for identifying patients with a high risk for coronary artery disease (CAD) since 94% of the subjects with high ox-LDL have cardiovascular disease. Many studies have shown that diets high in polyphenols reduce the susceptibility of LDL oxidation in CAD patients.<sup>110</sup> A diet providing 2, 3.5 and 5.5 ounces of raisins per day for 4 weeks lowered ox-LDL levels.<sup>98</sup>

***In conclusion, because of their high phenolic content, raisins are an important source of antioxidants in the diet. Raisins have higher polyphenol antioxidant content than Thompson Seedless grapes. In terms of their antioxidant capacity (as measured by H-ORAC) raisins are ranked within the highest quartile among fruits and vegetables. This is important because the antioxidant effect of polyphenols has been suggested as an explanation for the protective effect of fruits and vegetables. Raisins not only have high antioxidant capacity in vitro but also have been shown to raise blood antioxidant capacity and to protect against a marker of oxidative stress: oxidative damage to DNA and oxidation of LDL particles.***

## ii. Raisins and Cardiovascular Health

*Raisins are a good source of fiber and polyphenols in our diet. Both of these food components are important for cardiovascular health.*

Cardiovascular disease (CVD), primarily from heart disease (CHD) and stroke, is the leading cause of death in the United States for both men and women among all racial and ethnic groups. More than 850,000 Americans die each year from CVD accounting for nearly 40% of all deaths. The cost of heart disease and stroke in the United States in 2005 is estimated at \$393 billion, including health expenditures and lost productivity. These costs are expected to increase by 2010.<sup>111</sup>

Many studies have established that high plasma levels of total cholesterol and LDL cholesterol are among the most important modifiable risk factors for heart disease. While the mechanisms through which these factors lead to atherosclerosis and heart disease are not completely understood, evidence points to the oxidation of LDL particles by either free radical byproducts, or by mediators of inflammatory processes, as a probable causative process.

Large epidemiological studies, such as the Nurses' Health Study<sup>112</sup> and the Scottish Heart Health Study<sup>113</sup> show that individuals who consume diets high in fiber have a lower risk for heart disease. Soluble fiber may be of particular preventive value since it appears to lower plasma cholesterol levels. The mechanisms which may explain how fiber lowers serum cholesterol have been extensively reviewed and include: lower cholesterol absorption, higher bile acid excretion, changes in bile-acid type present in the intestinal tract, and influences of short-chain fatty acid production by intestinal flora.<sup>114 115</sup>

Epidemiological and experimental evidence suggests a protective effect of polyphenol-rich foods against CHD and stroke.<sup>116</sup> Polyphenols in fruits, vegetables and beverages may protect from atherosclerosis because of their antioxidant potential and through their anti-inflammatory activity. Flavonoids are known to react with a variety of disease promoting free radicals and to

induce antioxidant enzymes. While human data is limited, *in vitro* and *in vivo* studies have shown that many polyphenols, quercetin among them, and polyphenol-rich foods, inhibit LDL oxidation. They can modulate nitric oxide synthesis, promote vascular relaxation and inhibit platelet adherence to the vascular endothelium. Atherosclerosis is now viewed as a chronic inflammatory disease. Recent studies suggest that flavonoids protect from initiation and progression of atherosclerosis by modulating inflammatory pathways. They have been shown to inhibit mast cell secretion of pro-inflammatory cytokines and inhibit TNF-stimulated induction of endothelial cell adhesion molecules. Many excellent reviews on flavonoids and heart health have been published.<sup>117 118</sup>

***Raisins as part of a diet high in unrefined foods have been shown to have a beneficial effect on blood lipid levels.*** Spiller *et al*<sup>119 120</sup> were the first to study the hypocholesterolemic effect of plant-based diets, which included more than one serving of sun-dried raisins daily. They fed hypercholesterolemic adults Mediterranean-style diets high in whole grains and nuts, and that provided 84g raisins daily, for 4 weeks. By the end of the study total cholesterol and LDL cholesterol were 9% and 15% lower, respectively, than at baselines. There were no significant changes in HDL levels. Bruce *et al*<sup>121</sup>, in a crossover study, showed that a diet rich in unrefined foods, that also provided 126g of raisins daily, lowered total cholesterol and LDL cholesterol by 13% and 16%, respectively, in hyperlipidemic volunteers. In a randomized study, Gardner *et al*<sup>122</sup> showed that a plant-based, low-fat diet (which included raisins as snacks) significantly lowered total and LDL cholesterol levels among moderately hypercholesterolemic volunteers compared to those who consumed a more conventional, low-fat diet based on convenience foods. ***While many foods can account for the observed hypolipidemic effect of the experimental diets, these findings show that sun-dried raisins can be consumed as part of a cholesterol-lowering, plant-based diet.***

In a recent study, Puglisi *et al*<sup>123</sup> showed that raisins alone could have a beneficial effect on blood lipids. Thirty four volunteers were assigned to consume 1 cup of raisins daily, increase the number of steps walked in a day or a combination of both for 6 weeks. Raisins substituted

for other foods to ensure weight maintenance. Both interventions alone or in combination lowered plasma LDL cholesterol and increased LDL receptor expression (Table 12). Triglyceride levels did not change among the volunteers in the raisin and in the raisin and exercise group. This study also looked at the effect of these interventions on inflammatory cytokines. Subjects in the raisin group had significantly lower levels of TNF- $\alpha$  and sICAM-1. TNF- $\alpha$  is a powerful pro-inflammatory cytokine. Reducing TNF- $\alpha$  could potentially prevent progression of inflammatory damage. sICAM-1 is a cellular adhesion molecule. Lower levels of this sICAM-1 could potentially prevent progression of atherosclerosis by decreasing adhesion of monocytes to the vascular endothelium.

None of the diets containing raisins mentioned above increased triglyceride levels. This is important because it is often assumed that increasing intake of carbohydrates, often consumed in their refined, low-fiber form, and lowering intake of fat adversely affect serum triglycerides. However, carbohydrates rich in fiber and phytochemicals do not have this effect. Spiller *et al*<sup>124</sup> fed volunteers a typical Western diet for 3 weeks and then switched their diet to a NCEP (National Cholesterol Education Program) Step 1 diet supplemented with raisins and whole wheat raisin bread for 13 weeks. Triglyceride levels were 19% lower (non-significant) than baseline values. ***These results suggest that carbohydrates rich in fiber and phytochemicals such as sun-dried raisins do not increase triglyceride levels.***

Hypertension is a risk factor for heart disease. A recent study suggests that among individuals with mild hypertension, routine consumption of raisins significantly lower blood pressure when compared to eating other common snacks.<sup>125</sup> This randomized controlled clinical trial compared eating raisins 3 times a day to prepackaged commercial snacks that did not contain raisins but had the same number of calories for 12 weeks. Eating raisins significantly lowered systolic blood pressure at weeks 4, 8 and 12 compared to alternative snacks. Within group comparison showed that snacking on raisins lowered mean diastolic blood pressure at all study visits. Authors concluded that raisins are rich in potassium which is known to lower blood pressure. In addition raisins are a good source of antioxidants and dietary fiber that may

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favorably alter the biochemistry of blood vessel that may contribute a beneficial effect on blood pressure.

*In summary, raisins are a good source of both fiber (soluble and insoluble) and polyphenols. Raisins, as part of a diet high in whole and unrefined foods, have a beneficial effect on lipid levels. The addition of raisins to the a daily diet has been shown to lower total and LDL cholesterol levels, reduce markers of inflammation, increase plasma antioxidant capacity and lower circulating levels of oxidized LDL, a marker of coronary heart disease risk. Because of their high potassium content raisins may contribute to healthy blood pressure.*

**Table 12. Plasma total cholesterol (TC), LDL cholesterol (LDL-C), HDL cholesterol (HDL-C) and triglycerides (TG) of subjects consuming raisins (RAISIN), increasing walking (WALK) or both (RAISIN + WALK).<sup>1 2</sup>**

| Variable                      | TC<br>(mmol/L)     | LDL-C<br>(mmol/L)  | HDL-C<br>(mmol/L)  | TG<br>(mmol/L)     |
|-------------------------------|--------------------|--------------------|--------------------|--------------------|
| <b>Raisin (n = 12)</b>        |                    |                    |                    |                    |
| <b>Baseline</b>               | <b>5.21 ± 0.98</b> | <b>3.21 ± 0.84</b> | <b>1.56 ± 0.36</b> | <b>0.94 ± 0.47</b> |
| <b>6 Weeks</b>                | <b>4.82 ± 0.93</b> | <b>2.90 ± 0.76</b> | <b>1.53 ± 0.31</b> | <b>0.90 ± 0.35</b> |
| <b>Walk (n = 12)</b>          |                    |                    |                    |                    |
| <b>Baseline</b>               | <b>5.47 ± 1.37</b> | <b>3.16 ± 1.16</b> | <b>1.56 ± 0.50</b> | <b>1.49 ± 0.99</b> |
| <b>6 Weeks</b>                | <b>4.68 ± 1.12</b> | <b>2.48 ± 0.69</b> | <b>1.58 ± 0.41</b> | <b>1.20 ± 0.73</b> |
| <b>Raisin + Walk (n = 10)</b> |                    |                    |                    |                    |
| <b>Baseline</b>               | <b>5.25 ± 0.96</b> | <b>3.01 ± 1.11</b> | <b>1.71 ± 0.50</b> | <b>1.17 ± 0.53</b> |
| <b>6 Weeks</b>                | <b>4.96 ± 0.79</b> | <b>2.74 ± 0.71</b> | <b>1.66 ± 0.55</b> | <b>1.24 ± 1.54</b> |
| <b>Time effect</b>            | <b>P &lt; 0.01</b> | <b>P &lt; 0.01</b> | <b>Ns</b>          | <b>ns</b>          |
| <b>Group effect</b>           | <b>ns</b>          | <b>Ns</b>          | <b>Ns</b>          | <b>P &lt; 0.05</b> |
| <b>Interaction</b>            | <b>ns</b>          | <b>Ns</b>          | <b>Ns</b>          | <b>ns</b>          |

<sup>1</sup>Values are means ± standard deviation for the number of subjects indicated in parenthesis. Data were analyzed using repeated measures ANOVA. <sup>2</sup> Puglisi *et al.* Lipids in Health and Disease 2008 7:14.

### iii. Raisins and Cancer Prevention

*Cancer causes over 550,000 deaths each year, making it the second leading cause of death in the United States, after heart disease. Lung cancer accounts for the majority of these mortalities, while prostate cancer and breast cancer rank second among men and women, respectively, before colorectal cancer.<sup>126</sup> While these statistics are sobering, cancer is in part a preventable disease: it is estimated that nearly one-third of all cancer deaths in the United States could be avoided through appropriate dietary modifications. Raisins are fruits with unique nutrient value that offer a convenient step towards healthier eating.*

Epidemiological studies have consistently shown that diets rich in fruits and vegetables help prevent many types of cancer. The inverse association between fruit and vegetable consumption and cancer incidence is strikingly consistent, and has led organizations around the world to recommend that populations increase their daily intake of these foods. Many components found in fruits and vegetables have been proposed as candidates for the observed protective effects, such as soluble and insoluble fiber and, more recently, polyphenolic compounds, particularly flavonoids. ***Raisins are an important dietary source of both of these cancer-protective compounds.*** Health benefits of fiber in raisins, including its potential cancer protective effect, are discussed in section VII, iii.

Although it is not well understood exactly how flavonoids work in the body to prevent cancer, they appear to affect the various stages of carcinogenesis: cancer initiation, promotion and progression. Flavonoids are potent antioxidants *in vitro* and are able to scavenge a wide variety of reactive molecules that can harm cell constituents. They have been shown to repair DNA damage; modulate nuclear receptors and gene expression; stimulate or inhibit enzymes that detoxify or activate carcinogens,<sup>127</sup> and influence the cell cycle, signaling pathways<sup>128</sup> and angiogenesis.<sup>129</sup> A number of reviews have described the above mechanisms in detail.<sup>130 131 132</sup>

The main flavonoids present in raisins are the flavonols quercetin and kaempferol. Quercetin inhibits carcinogen-induced cancer in many animal models.<sup>i 133 134 135</sup> In cell culture studies, quercetin suppresses the growth of ovarian, prostate and breast cancer cells and inhibits proliferation of ovarian and lung tumor cell lines. The exact molecular pathways that explain these effects are yet to be established, but may involve stimulating the production of the anti-proliferative transforming growth factor  $\beta$ 1; inhibiting cell growth and inducing apoptosis (programmed cell death) in damaged cells.<sup>136</sup>

Despite considerable experimental evidence supporting the notion that certain flavonoids have anti-carcinogenic activity, data from human population studies are still limited. Reviews on epidemiological studies<sup>137 138</sup> conclude that, while there is only modest evidence that total flavonoid intake is inversely associated with cancer risk, the evidence is stronger for an association between the intake of quercetin and the risk for lung and colorectal cancers. Recent studies are consistent with this assessment. A population-based, case-controlled study in California showed that intake of certain flavonoids including catechins; epicatechins, quercetin and kaempferol were inversely associated with lung cancer risk among tobacco smokers, but not among non-smokers.<sup>139</sup> A large prospective, case-controlled study in Scotland found a 27% reduction in colorectal cancer risk in people with the highest quartile of flavonol intake when compared to those with the lowest intakes. The reduction in risk was 32% when comparing quercetin intakes.<sup>140</sup> A series of multi-center, case-control studies conducted in Italy between 1991 and 2005 analyzing the relationship between intake of the six main classes of flavonoids (isoflavones, anthocyanins, flavan-3-ols, flavanones, flavones and flavonols) and the risk of different types of cancers further supports a protective effect for flavonols. Investigators found a reduced risk of developing ovarian cancer,<sup>141</sup> breast cancer,<sup>142</sup> oral and pharyngeal cancers,<sup>143</sup> and colorectal cancer<sup>144</sup> with higher intakes of selected flavonoids including flavonols. No association was found for prostate cancer risk.<sup>145</sup> Investigators evaluating prospectively the

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<sup>i</sup> AOM-induced colon cancer in mice; DMBA-induced skin cancer in mice, in rats and in hamster buccal pouch; DMBA-induced breast cancer in rats; DEN-induced lung cancer in mice; 4-NQO-induced tongue carcinoma.

association between intake of flavonoids and colorectal cancer in 71,976 women from the Nurse's Health Study and 35,425 men from the Health Professionals Follow-Up Study found no significant association with intakes of flavonols, including quercetin and kaempferol.<sup>146</sup> The Multiethnic Cohort Study in Hawaii and California looked at the association between intake of three flavonols (quercetin, kaempferol and myricetin) and the incidence of pancreatic cancer among 183,518 participants.<sup>147</sup> While intake of total flavonols was associated with a significantly lower cancer risk, kaempferol showed the greatest preventive effect. It is noteworthy that in a prospective study of fatal pancreatic cancer among 34,000 California Seventh-day Adventists, the higher levels of dried fruit consumption (raisins, dates and other) were associated with a highly significant protective effect on pancreatic cancer risk ( $< 1$  times per month = 1.0; 1-2 times per month 0.47;  $\geq 3$  times per week 0.35, trend  $p = 0.009$ ).<sup>148</sup> These data provide support for the limited but growing epidemiologic evidence that certain flavonoids are associated with a lower risk of cancer. Therefore, foods rich in flavonoids may be important determinants of cancer risk in the population.

Only one animal study has investigated the anti-cancer effect of raisin-containing diets.<sup>149</sup> Dannenberg fed cancer-susceptible mice<sup>i</sup> diets made to contain 1% and 10% raisins for 70 days. Mice on the raisin diets had about one third less tumors ( $p < 0.047$ ) than mice on the control diets. There was no dose response since both concentrations caused similar tumor inhibition. The apparent effectiveness in preventing intestinal cancer could be due to their relatively high fiber content in addition to their flavonoid content.

***Diets high in fruits and vegetables have been associated with a lower risk of developing cancer and other chronic diseases. Over the years, many phytochemicals, bioactive compounds that contribute to these benefits, have been identified and studied. Scientists believe that it is the additive and synergistic effect of phytochemicals in fruits and vegetables that are responsible for their anticancer activity.<sup>150 151</sup> The benefit of a diet rich in fruits and vegetables is a result of the complex mixture of phytochemicals present in them. Raisins, with***

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<sup>i</sup> The Min/+ mouse develops multiple intestinal adenomas spontaneously.

*their unique combination of nutrients, polyphenols and fiber are an important ingredient of a dietary strategy for optimal health.*

#### iv. Raisins in Diabetes Management

Diabetes is the 7<sup>th</sup> leading cause of death in the United States. An estimated 20.8 million people in the US – 7% of the population – have diabetes, a serious, life-long condition. Overall, the risk of death among people with diabetes is about twice that of people without diabetes of similar age. Diabetes also increases the risk of heart disease and complications include damage to the retina, kidneys and peripheral nerves.<sup>152</sup> Controlling blood sugar levels and keeping these closer to normal values will lower the risk of disease and death from complications. Since dietary carbohydrates have the most direct impact on blood sugar levels, controlling the amount of carbohydrate consumed per meal is the focus of diabetes nutrition management.

Raisins, like all commonly consumed fruits, provide carbohydrates as the only caloric macronutrient, many questions arise as to when and how much fruit should be consumed. The American Diabetes Association recommends following a dietary pattern, which includes carbohydrates from fruits, vegetables, whole grains, legumes and low-fat milk, as well as monitoring dietary carbohydrates, whether by carbohydrate counting, exchanges (Table 13) or experience-based estimates, to achieve glycemic control.<sup>153</sup> The use of the Glycemic Index in addition to the consideration of total carbohydrate may provide an added benefit. Of course, frequent blood glucose monitoring is strongly recommended, as it indicates which foods, physical activities and/or meal times elevate blood glucose levels. Individuals diagnosed with diabetes should work with a registered dietician to create a meal plan that accommodates the patient's weight, medication, carbohydrate needs and lifestyle.

**Table 13. Exchange List for Dried Fruits <sup>†</sup>**

| <b>Dried Fruit</b>                        | <b>Serving Size</b>                             |
|---|---|
| <b>Raisins</b>                            | <b>2/3 oz about 45 raisins or 2 tablespoons</b> |
| <b>Apples</b>                             | <b>4 rings ¾ oz</b>                             |
| <b>Blueberries, cranberries, cherries</b> | <b>½ oz or about 2 tablespoons</b>              |
| <b>Apricots</b>                           | <b>¾ oz or about 8 halves</b>                   |
| <b>Figs</b>                               | <b>¾ oz or about 1 ½</b>                        |
| <b>Prunes</b>                             | <b>¾ oz or about 3</b>                          |

† One serving (exchange) of fruit contains about 15 grams of carbohydrate, no protein or fat, and about 60 calories. Fruits in the amounts listed equal one exchange.

As with the general population, people with diabetes are encouraged to consume a variety of fiber-containing foods. The nutritional guidelines proposed by the general public's healthy-lifestyle recommendations are also appropriate for those with type 2 diabetes. They are therefore encouraged to consume fruits, including raisins. It is no surprise then that raisins feature prominently in recipes promoted by the American Diabetic Association.<sup>154</sup>

## v. Glycemic Index (GI) of Raisins

*In addition to their high antioxidant activity and dietary fiber content, raisins have a low to moderate Glycemic Index – a measure of how a food affects blood sugar levels. These three factors are important tools in diabetes management.*

Raisins could be useful for both athletes and people with impaired glucose tolerance because they provide energy to fuel physical activity without causing excessive increases in the postprandial blood glucose or insulin response. The GI<sup>i</sup> is a measure of how a food affects blood sugar levels. The GI of raisins was first assessed at  $64 \pm 11$  (glucose =100)<sup>155</sup> in a study involving 6 healthy, non-diabetic individuals. A more recent study measured raisin GI and Insulin Index<sup>ii</sup> in 10 sedentary adults, 10 pre-diabetic individuals, and 11 endurance athletes.<sup>156</sup> The GIs, using glucose as the reference food, were  $49.4 \pm 7.4$ ,  $49.6 \pm 4.8$  and  $62.3 \pm 4.8$ , respectively (Figure 6). The Insulin Index was  $47.3 \pm 9.4$ ,  $54.4 \pm 8.9$  and  $51.9 \pm 6.5$  for these groups (Figure 7). This is important because high fasting and/or postprandial insulin levels can increase cholesterol synthesis and impair fat mobilization from adipose tissue. Kern *et al* calculated a raisin GI of 62<sup>iii</sup> in 8 endurance-trained cyclists, a value which is consistent with those above.

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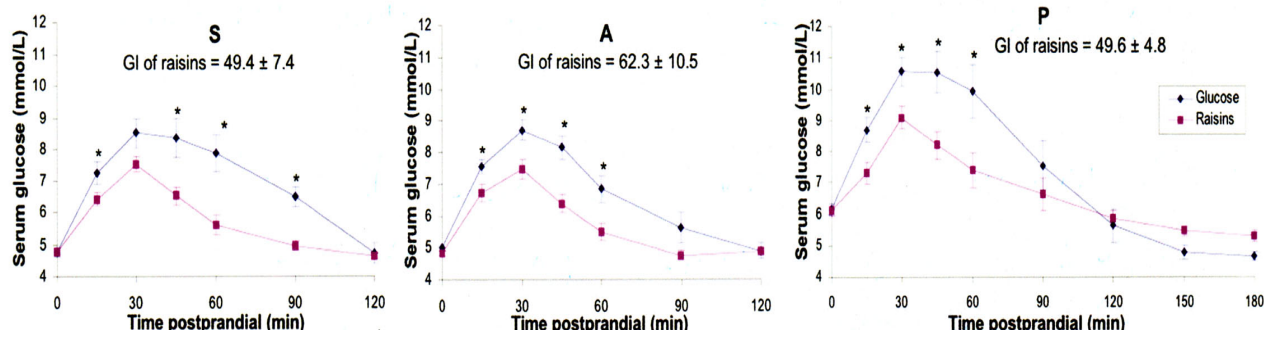
<sup>i</sup> The GI is determined by measuring the postprandial (2-3 hours) increase in blood glucose resulting from ingesting a portion of food containing 50 grams of available carbohydrate. The incremental area under the curve (AUC) is calculated for the test food and divided by the incremental AUC achieved from ingestion of 50 grams of carbohydrate from a reference food (i.e. white bread, glucose solution) and expressed as a percentage.

$$GI = \frac{\text{Blood glucose AUC from test food}}{\text{Blood glucose AUC from reference food}} \times 100$$

<sup>ii</sup> The Insulin Index is calculated in a similar way, though sometimes energy, rather than the carbohydrate content of the meal, is used to standardize the equation.

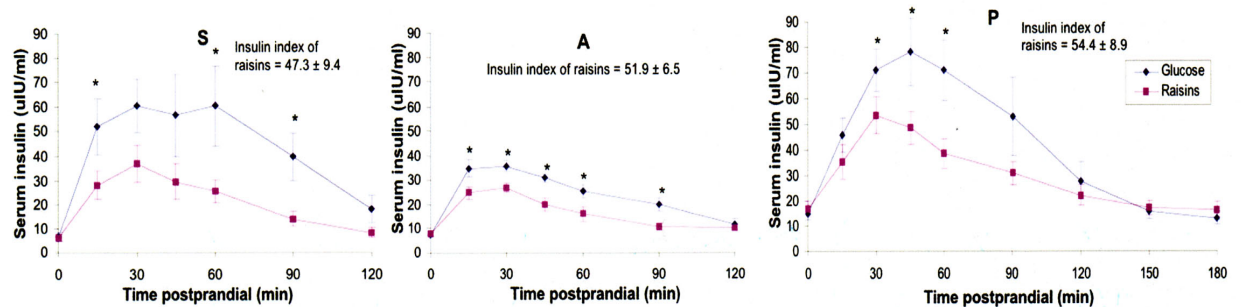
<sup>iii</sup> The actual raisin GI value was 88, obtained using white bread as a standard.

**Figure 6. Serum Glucose Responses to Raisins and Glucose in Sedentary Individuals, Athletes and Pre-diabetics**



\* Data points are means  $\pm$  SEM; Significant differences between glucose and raisins ( $p < 0.05$ )

**Figure 7. Serum Insulin Response to Raisins and Glucose in Sedentary Individuals, Athletes and Pre-diabetics**



\* Data points are means  $\pm$  SEM; Significant differences between glucose and raisins ( $p < 0.05$ )

A recent study shows that a 100 calorie serving of raisins has a similar glycemic response than that of an equivalent serving of bananas or grapes and a lower plasma insulin

response. In this study, fasting type 2 diabetics received 100 caloric servings of bananas, raisins, Thompson seedless grapes, raisins of white bread on each of four separate lab visits in a single cross-over fashion. Blood glucose and plasma insulin were measured before and after 30, 60, and 120 minutes of eating the snacks. There was no difference in the glycemic response to the raisin, bananas or grape snacks. Authors conclude that the favorable glycemic and insulin response coupled with the extended shelf-life and portability of raisins make them an attractive choice for improving fruit consumption among type 2 diabetics.<sup>157</sup>

Foods with high fiber content generally have a low GI. However, other factors also contribute to a food's glycemic response, such as the type of carbohydrate or sugar present, the physical characteristic of the food matrix and the presence of organic acids. For example, one study found considerable differences in blood glucose response between processed snack meals (chocolate-coated candy bar or a cola drink with crisps) and whole-food snack meals (raisins and peanuts or bananas and peanuts),<sup>158</sup> which were designed to provide equal amounts of fat and energy. Peak glucose concentrations tended to be higher after the candy bar snack and the cola drink snack than after either of the peanut snacks. Plasma insulin levels were significantly lower after the raisin-peanut snack than after the candy bar and cola drink snack. The area under the insulin curve (Table 14) was 68%, 75% and 52% lower after the raisin-peanut snack than after the candy bar, the cola drink and the banana-peanut snacks, respectively. The comparison between the raisin-peanut snack and the banana-peanut snack is particularly interesting, since both meals had similar total carbohydrate, sugar, fat and protein content. Factors thought to contribute to raisins' lower glycemic response were the viscous texture of its food matrix when chewed, the presence of tartaric acid and the type of sugar present (about 50% fructose).

***In conclusion, all studies assessing raisin GI show that raisins are a low to moderate GI food and that the insulin response is proportional to their GI. Moreover, a serving of raisins has the equivalent glycemic response as one serving of grapes.***

Table 14. Areas under the plasma glucose and insulin curves after different snack meals <sup>† ‡</sup>

| Snack Meal            | Glucose  | Insulin     |
|-----------------------|----------|-------------|
| Candy bar, tea        | 730 ± 26 | 3518 ± 406  |
| Cola drink, crisps    | 731 ± 27 | 3670 ± 275  |
| Raisins, peanut, tea  | 745 ± 26 | 2093 ± 284* |
| Bananas, peanuts, tea | 716 ± 26 | 3194 ± 202  |

<sup>†</sup> Mean ± SEM; <sup>‡</sup> Adapted from Oettle *et al.*

\*Significantly different than the other meals

## vi. Raisins, Polyphenols and Incidence of Diabetes

*Given the potential for flavonoids to protect the body against free radicals and other oxidative compounds, it is biologically plausible that consumption of flavonoids or flavonoid-rich foods such as raisins may reduce the risk of diabetes.*

Several small dietary intervention trials have shown that eating flavonoid-rich foods is associated with a significant increase in flavonoid levels in the blood of diabetic patients. Flavonoids are potent antioxidants because they function as free radical scavengers and metal chelators. It has been hypothesized that free radicals may contribute to autoimmune destruction of pancreatic  $\beta$ -cells, leading to diabetes and impaired insulin action. Flavonoids may preserve  $\beta$ -cell function by reducing oxidative stress-induced tissue damage and so protect against the progression of insulin resistance to type 2 diabetes.

Three large epidemiological studies have investigated the relationship between dietary flavonoids and development of type 2 diabetes. Knekt<sup>159</sup> examined the association between flavonoid intake and the incidence of a variety of chronic diseases, including diabetes, using data from the Finnish Mobile Health Examination Survey.<sup>i</sup> A lower risk of type 2 diabetes tended to be associated with higher quercetin and myricetin intakes. Adjustments for cardiovascular disease risk factors or dietary sources did not alter the results. However, the Women's Health Survey, a large prospective study of American middle-aged and older women, found no association between risk of type 2 diabetes and intake of either total or individual flavonoids as well as of most flavonoid-rich foods.<sup>160</sup> In a subset of 344 non-diabetic women, total flavonoid intake was not significantly related to plasma insulin levels. Results from this study are consistent with those from the Iowa Health Study of postmenopausal, predominantly white women where investigators found no association between flavonoid intake and the incidence of diabetes.<sup>161</sup> A possible limitation of these studies is the small variation in the participants' intake of flavonoids and flavonoid-rich foods. Also, flavonoids consist of more than 4,000 different compounds, but quantitative information is only available on a handful of them in food composition databases. Further research is evidently needed before firm conclusions can be drawn regarding the role of dietary flavonoids in the development of type 2 diabetes.

## **vii. Raisins, the Perfect Snack**

Snacks are an important part of a child's diet. Young children need more frequent meals than adults and need snacks between meals to support growth and development. However, the snack's nutritional value should take precedence over its caloric content. Overweight and obesity in children have become the most prevalent nutritional problem in the US. Since the

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<sup>i</sup> The Finnish Mobile Clinic Health Examination Survey conducted multiphasic screening examinations of 62,440 people, 40 years and older, in different regions of Finland during 1966 – 1972. Food consumption questionnaires were obtained from a random 10,054 participants, in addition to data on disease symptoms, medicine use and smoking habits. Flavonoid intakes were estimated from a database on flavonoid concentrations in Finnish foods.

1980s, the rates have doubled for children and tripled for adolescents. More than 15% of all 6 to 19 year olds are overweight. Childhood obesity is often referred to as an epidemic in both the medical and nutrition community setting.

A mid-morning and a mid-afternoon snack should be an opportunity to increase a child's intake of dairy, fruits and vegetables. A healthy snack will also cut down on the feeling of hunger and overeating at meal times. *The American Dietetic Association*<sup>162</sup> lists raisins among ***"The Perfect Snack," foods that provide energy and also help meet nutritional needs. The Committee on Nutrition Standards in Schools, in their recommendations for snacks, foods and beverages offered in schools, has designated raisins as a Tier 1 Food. Tier 1 Foods "provide important health benefits that warrant encouraging consumption by school-age children, and do not exceed levels of certain nutrients and compounds that may be unhealthful for school-age children when consumed in excess."***<sup>163</sup>

Healthy snacks should be promoted among children participating in sport activities. Too often children are provided with high sugar snacks and drinks, with little nutrient value beyond energy, that override the benefits of exercising. *Raisins either alone*<sup>164</sup> *or with nuts*<sup>165</sup> *have been shown to maintain steady glucose levels and support the demand for energy during sports activities in young soccer players. Moreover, eating raisins as an after-school snack prevents excessive calorie intake and increases satiety.*<sup>166</sup>

## viii. Raisins in Sports Nutrition

Carbohydrate-rich foods enhance endurance and performance when eaten either before or during exercise. They help promote carbohydrate availability and maintain blood glucose levels. Although not all studies agree, research suggests that pre-exercise carbohydrate snacks of low to moderate glycemic index (GI) are more effective in enhancing performance than high GI ones.<sup>167</sup> ***Raisins, an excellent source of carbohydrates and a moderate GI food, are the ideal pre-exercise snack to provide sustained energy and ensure optimal athletic performance.***

A recent study<sup>168</sup> compared raisins to a commercial, sucrose-based, high GI sports gel to see if one offered cyclists a performance advantage. Researchers fed endurance-trained cyclists the

equivalent of either 3 one-ounce gel packs or 2 small boxes of raisins, 45 minutes before exercising. Both snacks supplied about the same amount of carbohydrates (1 gram of carbohydrate per kilogram of body weight), to supply the readily available fuel needed for strength and endurance. Despite the differences in GI, both snacks elicited similar metabolic responses after 45 minutes of exercise. There was no difference in performance during a subsequent 15-minute exercise bout. The researchers concluded that raisins, being less expensive than sports gels and a source of naturally occurring nutrients, offer an advantage to those athletes desiring a “food first” approach to nourishment. Furthermore, they commented, the benefits of raisin-nut based trail mixes should be studied because research suggests that adding protein in post-exercise feedings may be useful during recovery.<sup>169</sup>

Another study compared running performance between males consuming water alone or a 240 calorie snack of either raisins or a commercial carbohydrate chew (Cliff Bar: 68% CHO, 16% fat, 16% protein).<sup>170</sup> Eleven competitive runners ( $29.3 \pm 7.9$  years of age) completed 3 randomized trials (raisins, chews and water only) separated by seven days. Each trial consisted of an 80 minute run at 75%  $\text{VO}_2\text{max}$  followed by a 5-km time trial. Raisins and chews promoted higher carbohydrate oxidation and improved running performance compared to water alone. The raisin treatment induced a lower energy contribution from CHO oxidation and a greater contribution from fat compared to the chew treatment. Running time for the 5 km time trial was lower by 1 minute with the raisin and chew treatments than with the water only treatment ( $20.6 \pm 2.6$ ,  $20.7 \pm 2.5$  and  $21.6 \pm 2.7$  respectively). There was minimal or no adverse gastrointestinal distress experienced during running by all treatment groups.

***Research shows that carbohydrate-rich foods fed prior to exercise enhance endurance performance. Raisins are a nutritious, cost-effective source of carbohydrate, an excellent choice to prepare an athlete for the upcoming activity.***

## ix. Raisins and Weight Management

There are no studies that have investigated the effect of eating raisins on weight management, however, three recent studies suggest that there may be a beneficial effect of a

high raisin diet and weight control.

***One cross-sectional study showed that people who eat raisins and other dried fruit are less likely to be overweight and have abdominal obesity than those who don't eat these fruits.*** <sup>171</sup>.

Investigators used the NHANES (1999-2004) data to examine the associations between dried fruit consumption and body weight and adiposity in adults (n = 13,292). For the purposes of the analysis, dried fruit eaters were defined as those eating greater than or equal to one-eighth (1/8) cup of fruit per day either out of hand or as ingredients within other foods. Those who ate dried fruit had higher energy intake than those who did not. However, mean body weight, BMI and waist circumference were all lower for those who ate raisins and other dried fruit. Moreover, after adjusting for potential cofounders, prevalence of overweight/obesity and prevalence of abdominal obesity were lower for those who ate raisins and other dried fruits than for those who did not.

The study by Puglisi described before showed that ***raisins could promote satiety by affecting the levels of hormones that regulate appetite.*** <sup>172</sup> Volunteers were assigned to consume 1 cup of raisins daily, increase the number of steps walked in a day or a combination of both for 6 weeks. Raisins substituted for other foods to ensure weight maintenance. While walking had no effect on hormones related to satiety, raisin consumption increased plasma leptin levels (Table 15). Higher leptin levels could promote satiety and decrease caloric intake. Leptin plays a key role in regulating energy intake and appetite. It is secreted by adipocytes in proportion body fat. It serves as a signal to the brain that the body has enough to eat.

**Table 15. Plasma leptin levels in the different interventions.**

| Interventions                     | Leptin (pg/mL)  |
|-----------------------------------|-----------------|
| <b>Raisins only (n = 12)</b>      |                 |
| Baseline                          | 6045 ± 4124     |
| 6 wk                              | 8330 ± 6630     |
| <b>Walking only (n = 12)</b>      |                 |
| Baseline                          | 11 950 ± 12 299 |
| 6 wk                              | 11 845 ± 10 536 |
| <b>Raisins + Walking (n = 10)</b> |                 |
| Baseline                          | 16 606 ± 16 587 |
| 6 wk                              | 23 578 ± 21 958 |
| Time effect                       | $P < .005$      |
| Group effect                      | $P < .05$       |
| Interaction                       | NS              |

Values represent mean ± SD for the number of subjects indicated. NS indicates not significant

A recent study looked at the effect of *ad libitum* after-school snack of raisins, grapes, potato chips or chocolate chip cookies on subjective appetite and food intake among children ages 8 to 11. Twenty six boys and girls were randomly assigned to eat raisins or other snacks until they were comfortably full. Additionally, each child received the same standardized breakfast, morning snack and lunch on test days. Subjective appetite was measured before and immediately after snack consumption at 15-minute intervals. *Ad libitum* snack consumption was lower, and satiety was greater after the raisins snack. Cumulative energy intake was lowest after

raisin consumption compared to the other snacks. Authors concluded that eating raisins as an after-school snack contributes to lower energy intake and subjective appetite and may promote the maintenance of healthier body weights in children.<sup>166</sup>

## x. Triterpenes, Raisins and Dental Health

***Raisins may promote healthy teeth and gums. Contrary to longstanding popular perception that raisins promote cavities, recent studies indicate that raisins may benefit oral health. Phytochemicals found in raisins may benefit oral health by fighting bacteria that cause cavities and gum disease.***<sup>173</sup> Oleanolic acid, oleanolic aldehyde and 5-(hydroxymethyl)-2-furfural have been shown to inhibit the growth of two species of oral bacteria: Streptococcus mutans, which cause cavities, and Porphyromonas gingivitis, which causes periodontal disease. These compounds were found to be effective at concentrations ranging from about 200mcg to 1,000mcg per ml. Two other compounds isolated from raisins, betulin and betulinic acid, also exhibit antimicrobial activity, but much higher concentrations are needed to achieve similar effects.<sup>174</sup> At concentrations of 31mcg per ml, oleanolic acid also blocks the adherence of S. mutans to experimental surfaces. This quality is significant because adherence is bacteria's first step in forming dental plaque, the film that accumulates on teeth.

Raisins have been thought of as cariogenic foods because they are sweet and sticky. However, recent research has shown that perceived "stickiness" bears little relationship to the actual retention of food particles on tooth surfaces (or objective measures of tooth retention) and the clearance of food-derived sugars from saliva.<sup>175</sup> In these studies, ***raisins have been shown to exhibit rapid clearing rates, placing them among the least retentive foods within a sample of 21 commercially available snack foods.***

A recent study specifically studied raisins and oral health in children aged 7-11 years.<sup>176</sup> In a randomized, controlled, cross-over study, researchers measured dental plaque acidogenicity after children ate raisins, raisin-containing cereal and cereal alone. The plaque pH was measured prior to and 2, 5, 10, 15 and 30 minutes after consumption of each food. Eating raisins alone did

not lower plaque pH below pH6 over the 30 minute test. This indicates that they did not lower plaque pH to the critical level that would increase the risk of caries. Addition of raisins to bran flakes promoted a smaller plaque pH drop beyond 10 minutes when compared to bran flakes alone. Raisins were less acidogenic than a raisin bran cereal, bran flakes or a 10% sucrose solution. This shows that raisins were less retentive on tooth surfaces and were rapidly cleared after chewing, and actually lowered the acidogenicity when added to bran flakes. They also enhanced clearance rate of the chewed particles so that they lowered acidogenicity when added to bran flakes.

Finally, *the predominant sugars in raisins are fructose and glucose, with minimal amounts of sucrose*. Studies comparing the cariogenicity of different sugars (sucrose, maltose, lactose, fructose and glucose) invariably demonstrate that sucrose, more than any other type of sugar, induces the most smooth-surface-type and fissure-type caries.<sup>177</sup>

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