

Chapter 2

Wolfberry Phytochemicals

What are Wolfberries?

Before we begin our examination of wolfberry nutrients, we want to fix a mental picture of this unique berry. On the front and back covers are pictures of wolfberries that we use as reminders of its characteristics while we move through the book. Sections later (Chapters 8,9) give more details about factors affecting wolfberry nutrients, such as its botanical family, soil and climate conditions, geographical harvesting regions, cultivation methods and other horticultural features.

Botanically, wolfberry belongs to the Solanaceae (“sole-an-eh-see-eye”) family, also referred to as nightshades or boxthorns. By scientific or Latin designation, it is called *Lycium barbarum* L. “Lycium”, the genus name, is thought to be from the ancient Mid-Asian geographic region of Lydia; barbarum, the species name, says its origin was “foreign” (perhaps external to China), and “L.” indicates the name derived from the Linnaeus taxonomy format.

The name for wolfberry in Mandarin Chinese is gou qi zi where “zi” means berry. By colloquial practice, the name has sometimes become abbreviated further to “goji” berry.

There are hundreds of nightshade plants in the large Solanaceae family, such as the tomato, potato, tobacco and petunia, so one can see that wolfberry fits into a plant group providing edible fruit from colorful leafy blossoms. In the genus of this species, Lycium, are dozens of plants (see Chapter 8) yielding berries on boxthorn or matrimony vines, some of them poisonous.

Wolfberry fruit, growing along branches of these 3-15 ft vines, is a berry oblong in shape, bright red at full maturity and very juicy (front cover). Along the banks of China’s Yellow River thousands of years ago when it was first documented as a favored food, wolfberries must have been a very tempting and easy to pick prize for travelers and early farmers.

Phytochemicals as Nutrients

Several factors must come together to endow an edible plant with high nutrition as wolfberry is reputed to have. These would include its phylogeny (or plant “family tree”) determining its genetic endowment, environmental conditions of soil, weather, growing season, exposure to pests, cultivation methods and so on.

All these factors merge in wolfberry to establish a unique nutrient profile. A plant such as wolfberry may contain a variety of nutrients including those chemicals unique to its own makeup, giving it nutrient “signatures” that stand out among other berries or any edible plant. As we discuss later, wolfberry’s signature nutrients are two classes of interesting and health-promoting phytochemicals – polysaccharide sugars (Chapter 4) and carotenoid pigments (Chapter 5).

A relatively new term in nutrition research is called “phytochemical” which means “plant-derived” chemical. Wolfberry is a fruit packed with phytochemicals, likely dozens of them in every berry. When nutritional properties are eventually known, phytochemicals will be referred to as phytonutrients.

And that is the primary goal of this book – to identify, organize and substantiate the scientific basis for wolfberry’s great variety of phytochemicals that serve as nutrients.

Not only in plants are there large or “macro” nutrient classes in gram quantities like carbohydrates, proteins, fiber and fat but also smaller amounts of “micro” nutrients in milligram or microgram quantities. These include vitamins, minerals, amino acids and interesting groups of other promising chemicals such as carotenoids, phenolics, phytoestrogens, fatty acids and sterols.

Let’s gain some perspective on phytochemicals from the Position Statement of the American Dietetic Association, 1995, entitled *Phytochemicals and Functional Foods*

In addition to the nutrients that are involved in normal metabolic activity, foods contain components that may provide additional health benefits. These food components (generally referred to as phytochemicals) are derived from naturally occurring ingredients and are actively being investigated for their health-promoting potential. Health benefits of these foods are best obtained through the consumption of a varied diet using our normal food supply.

These phytochemicals and/or health-preserving elements are present in a number of frequently consumed foods, especially fruits, vegetables, grains, legumes, and seeds, and in a number of less frequently consumed foods such as licorice, soy, and green tea. In addition, functional foods, which are defined as any modified food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains, are being developed and subjected to scientific evaluation. In recent years, the number of functional foods that have potential benefits for health has grown tremendously. Scientific evidence is accumulating to support the role of phytochemicals and functional foods in the prevention and treatment of disease.

The benefits of phytochemicals and functional foods have been extensively publicized in the popular press, resulting in increased public awareness and interest in consumption of phytochemical-rich foods and functional foods as a method of enhancing health and well-being. Although scientific evidence of clinical benefits is limited, evidence is mounting to support the incorporation of foods rich in phytochemicals into the diets of most Americans.

Although other accounts of phytochemical values to health have been published since 1995, this ADA advisory gives us good background for understanding the place in our diets for natural products like wolfberries.

It’s valuable, therefore, to consider nutrients and phytochemicals of wolfberries as available science allows. That is the goal of this and following chapters as we begin to unravel wolfberry’s nutrient profile.

Science-based guidelines for all phytochemical intake levels are not yet fully established although there are now government and expert panel advisories on intakes for vitamins, minerals and fiber. Watchdogs for public consumption of foods and specific nutrients, e.g., the US Department of Agriculture, US Food and Drug Administration, or Health Canada as western examples, have not yet published intake guidelines for all phytochemicals, saying there is insufficient research upon which to make recommendations.

This means science and clinical research have not yet laid sufficient foundation for the long-term benefits of phytochemicals, even if we do have growing evidence for the values of including more phytochemicals in our diets. As a result, their intake has not yet been defined as “essential” in the diet.

Excellent guidelines in popular media are emerging, however. One with relevance and background for this discussion of wolfberries is the 2004 book by Steven Pratt, MD and Kathy Matthews, *SuperFoods Rx*, describing 14 superfoods easily found in grocery store produce sections. As we’ll see later in our discussion, the Pratt and Matthews information on blueberries, spinach and flax seeds as common superfoods gives great background for better understanding wolfberries or any nutrient-rich food.

There may be as many as 8,000 individual phytochemicals among natural foods, with dozens occurring in a single nutrient-dense plant like the flax seed or wolfberry. These chemicals are more than just calories, vitamins, minerals or fatty acids – some are simple pigments that may offer broad health benefits preventing or delaying onset of diseases and effects of aging.

Simply with that message is a glimpse of why wolfberries have been popular in China for dozens of centuries and why we are motivated to write this book.

One fact from nutrition research on phytochemicals is clear, however. Consumption of the *whole* food (or perhaps a comprehensive nutritional supplement) guarantees intake of as many of the intact phytonutrients as possible. Once inside our bodies, the macro- and micronutrients can act in concert and so complement one another, a process some nutritionists refer to as *nutritional synergy*.

Such synergy may in fact explain wolfberry's numerous potential health benefits. For example, wolfberry's famous polysaccharide sugars are not only immunologically active (Chapter 4). They are also a major source of dietary soluble fiber that may

- 1) enhance calcium, magnesium and iron absorption,
- 2) help stabilize blood glucose (sugar) levels after a meal,
- 3) contribute to lowering blood cholesterol,
- 4) promote colon health by increasing production of fatty acids and raising acidity levels, thereby reducing colon cancer risk and
- 5) afford immune protection through a comprehensive array of intermediate effects within the intestinal system.

We'll devote more attention to synergy later in this chapter.

Until we have the full story about such minute interactions between numerous phytonutrients in a single food like wolfberry, one conclusion seems clear -- the safest and most effective way to benefit from wolfberry's bounty of nutrients is to eat the whole fruit, including its skin and seeds. We will need to consider, therefore, that the wolfberry juice products popularized on the internet and through multi-level marketing companies may omit beneficial phytonutrients left behind in the pomace from the juicing process (Chapter 10).

Another factor we'll consider in Chapter 10 is the processing of a multinutrient source like wolfberry for its individual extracts. Treatment of fruit pulp with solvents like alcohol, acetone, mild acids, heat and even simple mechanical methods can de-nature and/or diminish amounts of phytochemicals.

Simply, processing of a fruit to powder or juice may reduce its overall phytochemical value by minimizing the nutritional importance of skin and seeds. Eating the whole fresh or dried fruit likely provides optimal benefits.

Phytochemicals for Health

Medical studies to date have demonstrated that phytochemicals in common fruits and vegetables can have overlapping mechanisms of action, including such beneficial effects as

- antioxidant activity and scavenging free radicals
- regulation of gene expression in cell reproduction and repair, cell differentiation, and stimulation of cancer and tumor-suppressor genes

- induction of normal and abnormal cell death mechanisms (apoptosis, pronounced “eh-poe-toe-sis”)
- modulation of enzyme activities
- stimulation of immune system responses
- regulation of hormone metabolism
- antibacterial or antiviral mechanisms

As evident from this incomplete list, dietary phytochemicals enter into countless cell activities involved in moment-to-moment life and long-term health. To put it another way, ingestion of mixed phytochemicals through a diet of whole foods may be important to prevention of as many as 60 diseases related to the list above.

Why minimize such a valuable set of nutritional benefits by focusing on just one or a few extracts from a food source, as so many supplement products propose to do?

“Superfoods” as discussed by Pratt and Mathews have been given credit for providing all these health benefits in a convenient package *as the whole food*.

As we move through the book, we’ll examine pertinent research publications and offer interpretations where science is adequate to support claims of whole food nutrient synergy and how wolfberries may supply this benefit.

Phytochemicals, Antioxidants and Cancer

Cells in humans and other organisms are constantly exposed to a variety of oxidizing agents, some of which are necessary for life. These agents may be present in air, food, and water, or they may be produced even by normal metabolic activity within our cells.

Some are called “free radicals” or specifically “radical oxygen species” (ROS), meaning a reactive chemical such as singlet oxygen (O₁) formed when one atom of oxygen leaves the stable gas, O₂. A key health factor is to maintain a delicate balance between oxidizing agents and food-derived antioxidants to sustain optimal physiological conditions in health.

Overproduction of oxidizing chemicals or leaving them unchecked due to poor nutrition can cause an imbalance, leading to a condition called *oxidative stress*, especially in chronic diseases. Oxidative stress can cause damage to cell components like lipids important in cell membranes, proteins, and cell DNA affecting our genes, resulting in an increased risk for cancer cell development and potential onset of other diseases.

To prevent or slow oxidative stress induced by free radicals, sufficient amounts of dietary antioxidants need to be consumed. Fruits, vegetables, whole grains, seeds and nuts contain a wide variety of antioxidant compounds, such as phenolic acids and carotenoid pigments (Chapter 5), that may help protect cellular systems from ROS and so lower risk of chronic diseases.

Medical research and nutritional studies have shown that regular consumption of fruits and vegetables can reduce cancer risk via these antioxidant mechanisms.

One analysis of some 200 epidemiological studies examined the relationship between intake of fruits and vegetables and cancer of the lung, colon, breast, cervix, esophagus, mouth and throat, stomach, bladder, pancreas, and ovary. The consumption of fruits and vegetables was found to have a significant protective

effect on cancer development in these body organs.

Risk of cancer was higher in persons with a low intake of fruits and vegetables than in those with a high intake. Fruits were significantly protective in cancer of the esophagus, mouth, and larynx (throat). Combined fruit and vegetable intake was protective for cancer of the pancreas, stomach, colon and bladder.

The initiation of cancer is a multistep process and oxidative damage is linked to the formation of tumors through various mechanisms. Oxidative stress causes cell DNA damage, which if unrepaired, can lead to genetic mutations and cell structure breakdown or rearrangement of cell components. This potentially cancer-inducing oxidative damage might be prevented or limited by dietary antioxidants found in fruits and vegetables.

As we shall see in Chapters 4-6, wolfberries have been studied by Chinese scientists over the past 30 years as a possible preventative for these effects.

Antioxidants

We have mentioned the word “antioxidant”, to be given more in depth coverage in Chapter 5, as this is an important phytochemical category thought to be a major characteristic of wolfberries.

What are antioxidants and their potential health benefits? Antioxidants are substances synthesized in the body or obtained via food nutrients that can prevent or slow oxidative damage to our body’s cells.

Scientists believe that plants make antioxidants especially as pigments in their fruit skin, rind and seeds to protect the plant’s regenerative capacity from the damaging effects of constant exposure to sunlight, ultraviolet radiation, pests and oxygen.

Antioxidant phytochemicals such as blueberry anthocyanins contribute blue-purple pigment to the berry skin, and so play a useful role in attracting insect pollinators and birds that eat the fruit then disperse seeds in their droppings. Plants also would benefit from antioxidant protection in the skin against photo-oxidative processes, viral or bacterial pathogens, benefits that can be passed on to animals consuming the berry.

Without protective antioxidants from pigments like carotenoids and anthocyanins in plant skin, reactive oxygen species could be created during normal photosynthesis leading to oxidative injury to proteins, lipids and nucleic acids, alteration in gene transcription, and even programmed cell death (“apoptosis”) in the fruit or its seeds. Some botanists and food chemists refer to this protective benefit as “*pigment power*” desirable to obtain through the diet. For humans, this occurs by eating colorful fruits, vegetables and animal sources and so gaining the benefits of pigment power.

When human cells use oxygen, they naturally produce free radicals as by-products of normal metabolism that can lead to cell damage if normal counter-balances are not present in the environment inside and around our cells.

Antioxidants synthesized internally or those we obtain from our diets act as neutralizing sponges or “free radical scavengers”. They counterbalance, absorb, quench, prevent or repair damage done by free radicals. Health problems such as heart disease, hypertension, macular degeneration of the eyes, diabetes, cancer, and inflammation are influenced to some degree by oxidative damage and, apparently, by insufficient amounts of internal and dietary antioxidants.

As we study wolfberries and other fruit, vegetables and herbs with antioxidant properties, we shall see the enormous variety of antioxidant phytochemicals thought to number many thousands across the plant world.

Two classes that characterize darkly-colored berries, however, are the primary antioxidant class of phenolic acids or polyphenols, i.e., the numerous phenolic species common in blueberries, black raspberries, pomegranate and acai. Later in the book to provide simple terminology, we refer generally to all polyphenolic compounds as “phenolics”.

Carotenoids, a separate phytochemical class providing intense antioxidant activity, are abundant in wolfberries, discussed in Chapter 5.

An example of the nutritional and anti-cancer values of antioxidants from the scientific literature:

Publication. J Nutr. 2004 Dec;134(12 Suppl):3479S-3485S. **Potential synergy of phytochemicals in cancer prevention: mechanism of action.** Liu RH. Department of Food Science, Cornell University, Ithaca, NY, USA.

Abstract. Epidemiological studies have consistently shown that regular consumption of fruits and vegetables is strongly associated with reduced risk of developing chronic diseases, such as cancer and cardiovascular disease. It is now widely believed that the actions of the antioxidant nutrients alone do not explain the observed health benefits of diets rich in fruits and vegetables, because taken alone, the individual antioxidants studied in clinical trials do not appear to have consistent preventive effects. Work performed by our group and others has shown that fruits and vegetable phytochemical extracts exhibit strong antioxidant and antiproliferative activities and that the major part of total antioxidant activity is from the combination of phytochemicals.

We proposed that *the additive and synergistic effects of phytochemicals in fruits and vegetables are responsible for these potent antioxidant and anticancer activities and that the benefit of a diet rich in fruits and vegetables is attributed to the complex mixture of phytochemicals present in whole foods.* This explains why no single antioxidant can replace the combination of natural phytochemicals in fruits and vegetables to achieve the health benefits. The evidence suggests that antioxidants or bioactive compounds are best acquired through whole food consumption.

Synopsis. Systematic studies of large groups of people allow inferences about population masses (“epidemiological studies” or “clinical trials”). These studies show that eating whole foods rich in antioxidant nutrients provides a “synergy” of benefits for reducing cancer risk.

Such information is supported by other authors with two points we emphasize in this book: 1) consumption of a whole fruit (or other food source rich in nutrients) is likely to confer the greatest nutritional benefit and 2) choice of high-nutrient, high-antioxidant foods can help establish a base for good lifelong nutrition and health (also see Pratt and Matthews, 2004).

As we hope to provide the reader with as much information about wolfberries as available in present literature, one goal is to methodically identify nutrients conferring potential health value (Chapters 3 and 6). We also wish to compare wolfberry’s nutritional profile to those of other well known, nutrient-dense foods. Accordingly, the next chapter will be used to detail these nutrients and comparisons.

Wolfberry Nutrients and Possible Health Benefits

Wolfberry is a native Chinese plant used in traditional Chinese medicine for 5,000 years but with little international export until recently. As a result of this limited economy and lack of western science applied to wolfberry research, the plant is hardly known outside Asia. Exotic natural products from around the world are increasingly entering the mainstream of health foods in first-world countries so it is timely to consider nutritional benefits wolfberry may eventually offer to western diets.

Wolfberry fruit, seeds, leaves, roots and bark have been used by the Chinese for centuries in many herbal formulas to maintain overall health against fatigue, visual degeneration in aging, headaches, insomnia, inflammation, chronic liver diseases, diabetes, tuberculosis, hypertension and a host of other ailments outlined further in Chapters 6. For centuries, Chinese shamans and herbalists have advised use of wolfberry to make tea, soup, stew and wine or suggest chewing dried berries as snacks like raisins for daily maintenance of general health.

Legendary stories of its health benefits have established wolfberry as a Chinese national treasure revered over centuries as a fountain of youth.

What is known about wolfberry in the western world today, however, is mainly from unscientific misinformation published on the internet to promote juice products -- Goji Juice and NingXia Red Juice (a product new in 2005 previously called Berry Young Juice).

Summarized from web publications by the two manufacturers are potential health benefits of wolfberry juice

1. Extends life, protects against premature aging, has powerful antioxidant actions
2. Increases energy and strength
3. Stimulates secretion of human growth hormone and promotes youthful appearance
4. Maintains healthy blood pressure
5. Reduces blood cholesterol levels
6. Promotes normal blood sugar levels in diabetes mellitus
7. Enhances sexual functions and improves fertility
8. Helps lose weight
9. Relieves headaches and dizziness
10. Relieves insomnia
11. Supports eye health
12. Strengthens the heart and cardiovascular system
13. Improves disease resistance, strengthens immune responses, protects cellular DNA
14. Builds strong blood
15. Supports a healthy liver and pancreas
16. Treats menopausal symptoms
17. Prevents morning sickness during the early phase of pregnancy
18. Strengthens muscles and bones
19. Improves memory
20. Supports normal kidney function
21. Relieves chronic cough
22. Alleviates anxiety and stress
23. Promotes cheerfulness

What a list of possible benefits from the juice of just one fruit! It is likely, however, that these anticipated health benefits were extrapolated from findings of preliminary Chinese research or traditional Chinese practices where the whole fruit was used in diets and remedies. Observations on just a few people may have been magnified to infer large-scale comprehensive benefits. Consequently, we need to inspect that background carefully and objectively, a goal of this book.

Let's note that NingXia Red Juice (a wolfberry puree of berry pulp, skin, seeds and stem) is made to include juices of other nutritional berry fruits, such as the popular and scientifically validated blueberry and pomegranate. NingXia Red also contains orange and lemon essential oils, both of which contribute potent antioxidant qualities. A 2005 booklet by H. Rodier, MD extols the numerous potential health values of NingXia Red Juice, but is not founded on published clinical science.

Nevertheless, although no clinical publications exist on the health benefits of wolfberry juice, there is a growing popular following based sparingly on science and mainly on a large amount of tradition, Chinese lore, appealing taste and effective multilevel marketing.

With the present book, we do not intend to debate these health claims associated with the juice products. In fact, we have a goal to examine the limited scientific information about wolfberry as objectively as possible and to impartially consider health effects inferred from Chinese legends and juice manufacturers. We hope to balance our presentation by using as much information from peer-assessed medical literature as possible.

If some of these health benefits are eventually verified by the appropriate scientific rigors and agreement among experts, then the basic knowledge we hope to provide about wolfberry and its potential use as an ingredient in diets, health-promoting foods and supplements is a worthwhile outcome of this book.

Our main goal is to take a fair view of available information and Chinese lore about this ancient revered plant and help create objective facts to better understand wolfberry's nutrients and phytochemicals. Hopefully, this will provide a good review of the nutrient power wolfberry consumption may contribute toward health.

We shall examine some of the above claims in light of available science. As much of the information on wolfberries comes from Chinese institutions and authors who published only in the Chinese language, western science has had little to advance our understanding to date and has not undertaken many cross-validation studies. Wolfberry has simply not yet caught the imagination of western scientists to undertake a stream of research that would rigorously inspect and test the Chinese data.

Peer-Review for Functional Foods

According to the way in which peer review works, one scientific finding – even if published and accepted by traditionalists years ago in China, should lead to further examination, confirmation, dispute or refute by others. That is how good science is put to the test of scrutiny. One successfully tested idea usually leads to a new one that spawns another, and so on until there is cross-confirmation and general scientific acceptance of given facts.

In 2005, the Institute of Food Technologists published a review by scientific experts of the functional food industry (references, Chapter 12), outlining requirements for establishing credibility of claims about the health benefits of a food or juice such as wolfberry.

Functional foods are those natural or supplemented foods that contain one or more components (nutrients or phytochemicals) imparting a health benefit.

Experts must agree that a “claim is valid based on the totality of publicly available scientific evidence, including evidence from well-designed studies conducted in a manner consistent with generally recognized procedures and principles.”

The standard of scientific validity for a health claim includes two components: 1) that the totality of the publicly available evidence supports the substance/disease relationship that is the subject of the claim, and 2) that there is significant scientific agreement among qualified experts that the relationship is valid.

As that chain of proof has not yet been fully established for wolfberry’s profile of nutrients and associated health claims, we are reserved about what can be stated.

Therefore, our approach in the book will be to identify available information on wolfberries and present it uninfluenced by commercial motivations.

Value of Clinical Trials

Without belaboring our points above, let’s discuss briefly why food and medical research needs the clinical trial system to establish facts about nutrients and health.

Three main factors of a clinical trial that lead to acceptance of facts from nutritional research are 1) that a large number of people, perhaps hundreds or even thousands, have served as subjects, this number representing an even larger population segment (millions of users of the food under study), 2) that the design of the trial, especially its control of dietary or pharmaceutical factors that would influence or disguise the desired result, have been well controlled, and 3) that the results and interpretation of the data have been assessed objectively and reviewed rigorously by other experts (“peers”) before publication.

In clinical research on a new drug for treating a medical condition that affects millions of people, these factors are obviously important. Especially the trial design is crucial, but, by nature of the drug being entirely novel to use in people, control of diet or other drugs is relatively easy to establish.

This is not the case in food research where nutrients from many dietary sources can interact and/or conflict with the proposed beneficial nutrients under study. Consequently, it’s difficult (perhaps impossible) to establish sufficient experimental conditions for good clinical research on a food source with multiple nutrients affecting health or disease in varied ways.

Some food regulatory authorities, such as the US Food and Drug Administration and the Natural Health Products Directorate of Health Canada, are trying to overcome these problems for clinical trials on food and nutritional products. Chapter 2 references are given in the bibliography, Chapter 12.

Particularly, the Institute of Food Technologists report suggests that a weight of scientific evidence be constructed from 1) epidemiological studies, i.e., large-scale observational data associating foods and disease alleviation, 2) biological mechanisms revealed from chemical, cellular or animal models, and 3) intervention clinical trials of a food on a well-controlled sample of human users.

This preamble about clinical research is provided as background for the upcoming discussions on wolfberry nutrients, especially in Chapters 3-6.