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RE: Historical Use of Arginine for Scurvy

Durzan DJ. Arginine, scurvy, and Cartier's 'tree of life.' *J Ethnobio Ethnomed*. February 2, 2009;5:5. Available online at: http://www.ethnobiomed.com/content/5/1/5.

The crews of three French ships, suffering from scurvy near present-day Quebec City in the winter of 1536, were cured with an Iroquois medicine made from bark and leaves of a local conifer. The Iroquois referred to the tree as Annedda, while "other tribal names for conifers were "ohnehta" for white pine and "onita" and "onnetta" for white spruce (Mohawk, Orandaga). Seasonal and diurnal amino acid analyses show that ascorbic acid (vitamin C) and high levels of arginine, proline, other amino acids, and guanidine derivatives were probably present in conifer decoctions at that season and latitude. Spruce buds (*Picea* spp.) and jack pine (*Pinus banksiana*) seedlings are rich in amino acids, proteins, and nucleic acids. Hypotheses are presented for nutritional, synergistic roles for arginine, its metabolites, and other biofactors, with vitamin C, in curing explorer Jacques Cartier's men.

The 1536 incident benefited future naval exploration, and Cartier's gift of eastern white cedar (*Thuja occidentalis*) seeds to King François I sparked renewed interest in botany, as distinct from pharmacy. Confusion about the identity of the tree actually used began with the contemporary accounts, and none has been conclusively identified. While the branches are said to have come from a tree "as big as any oak in France," there is no evidence that Cartier or his men saw them collected. Other candidate trees, based on accounts by other explorers and the ethnomedicine of eastern Canada, include white spruce (*P. glauca; P. canadensis*), black spruce (*P. mariana*), eastern or five-needled white pine (*Pinus strobus*), red pine (*P. resinosa*), balsam fir (*Abies balsamea*), eastern hemlock (*Tsuga canadensis*), and juniper (*Juniperus communis*).

In nitrogen (N)-poor forest soils, lacking fertilizer, arginine is the main source of N for boreal conifers. Fir (*Abies* spp.), spruce, and pine (*Pinus* spp.) needles have 2.5 to 8.8 mg protein/100 g fresh weight. In a severe winter, at a latitude similar to present day Quebec,

buds and shoots of white spruce produced 150-200 mg amino acids/100 g fresh weight. In November, arginine in total soluble amino acid increased from 20% to 45%, and in February, with temperatures averaging -16°C, was 30-43%. In conifer seed protein, arginine may represent up to 10% of N. Nitrous oxide (NO) from arginine is produced in bursts in stressed conifers. Arginine is "a pivotal departure point from the urea cycle" for synthesis of urea and ornithine and is a substrate for formation of NO and citrulline via NO synthase (NOS), for guanidino compounds, and in protein synthesis. NO contributes to apoptosis and autophagy. NO production from arginine was "a significant evolutionary advance in gymnosperms before angiosperms and humans evolved." Plant NOS, still incompletely characterized, is different from human NOSs.

In humans, however, arginine is also a source of NO. In both humans and conifers, gaseous NO transmits signals from a cell, through membranes, to regulate activities of other cells. Treating scurvy with increased NO would affect a series of changes over time. In tissues, NO regulates oxygen release from red blood cells. It protects the heart, stimulates the brain, and regulates inflammation. It improves circulation, aiding distribution of amino acids, antioxidants and vitamins. It scavenges cytotoxic free radicals. It is involved in transmission of messages between nerve cells connected with memory, sleeping, and learning, and by improving these functions would help prepare the recovering sailors for an arduous return voyage. As an added benefit, NO would kill almost all bacteria swallowed with food.

Arginine-derived guanidino compounds prevent overproduction of NO, associated with septic shock, neurodegeneration, and inflammation. Some have been extensively researched as drugs. Guanidino compounds have been used as respiratory inhibitors, antibiotics, markers for metabolic disorders, and in studies of cardiovascular diseases and bacterial activity. They have been used to treat botulism, viral diseases, diabetes, and paraneoplastic syndromes. Synthetic guanidines are also used to treat diabetes. Guanidine, guanidinosuccinic acid, and creatine are elevated in uremia patients' tissues and fluids. Guanidino compounds are implicated in hypertension, hemorrhagic shock, seizure, renal dysfunction, and immersion stress.

Humans need vitamin C to efficiently use carbohydrates, proteins, and fats. Vitamin C protects against free radical damage and is essential in making collagen, the body's major building protein. Dietary deficiency, especially in long periods of cold, leads to scurvy, an acute chronic disease characterized by anemia, hemorrhagic skin lesions, hemorrhages in the musculoskeletal system, edema in lower extremities, bleeding gums and loosening of teeth. Scurvy in adults is treated with ascorbic acid at 300-1000 mg/d. Without treatment it is fatal. The disease, unknown to the French before Cartier's voyage, was prevalent in winter among the Iroquois. Vitamin C is found in fresh conifer tissues even in winter. Needles and bark of several species have more vitamin C than lemons (*Citrus x limon*) or oranges (*C. sinensis*). While large losses of vitamin C occur on heating, as in decoction (boiling water) preparation, the author believes the Iroquois scurvy medicine would have contained sufficient vitamin C, along with essential amino acids, conditionally essential arginine, and other biofactors to affect a cure.

One of Cartier's men wrote that, at first, none would try the strange drink. The first who eventually did so felt immediately better, and after two or three doses on alternate days were regaining strength and health. Dregs of the decoction were also applied directly to swollen legs. A rumor that the decoction would cure "all other diseases" brought the sailors, some of whom had syphilis, in a rush for the medicine.

Twenty-five conifers were traditional food sources for indigenous peoples in eastern Canada, many from the cypress (Cypressacae), pine (Pinaceae), and yew (Taxaceae) families. Both eastern hemlock and black spruce were dietary antiscorbutics with roots, twigs, leaves, and bark taken in daily decoctions. Teas made from conifer leaves were both refreshing drinks and medicinal tonics. Bark was usually collected from roots or branches on the east side of trees, believed more potent from sunlight. Green conifer tissues have high moisture content, vitamin C, folic acid, minerals, and other biofactors. The roots are a good source of minerals. Seeds, buds, cambium, and sap of candidate trees of life were all eaten. Inner bark of trees was an emergency food at any time of year.

Conifer bark contains many bioflavonoids and proanthocyanidins. The Algonquins used white pine decoctions for breathing disorders, rheumatism, and kidney problems. The Iroquois used spruce species for respiratory ailments, urinary problems, and as a poultice for blood poisoning. An antioxidant proanthocyanidin from French maritime pine (*P. pinaster*; *P. maritima*) bark, Pycnogenol® (Horphag/NHS; Berlin, Germany), is in clinical trials for lymphedema, endothelial function in coronary heart disease, hypertension, and diabetes. Indigenous peoples used yew (*Taxus* spp.) decoctions to treat fever, scurvy, bring out clots and relieve pain after childbirth. Yew species produce over 300 taxanes, the best-known of which today is the anticancer drug paclitaxel (Taxol®; Bristol-Myers-Squibb; New York). Herbal remedies made from eastern Canadian conifers also contain salicylates, astringent tannins, acetylenes, antibacterial alkaloids, and anti-inflammatory terpenes.

The author points out that the boiled decoction that cured Cartier's crews would also have been likely to contain tree lichens (e.g., edible horsehair [*Bryoria fremontii*]), adding complex polysaccharides and other nutrients and vitamins to the medicinal broth.

-Mariann Garner-Wizard

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