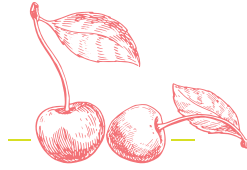


NORTHWEST CHERRIES

More
than just
Great
Taste

Northwest
Cherries





Recent years have seen a surge in the research of cherries, delving beyond nutritional value to expose deeper health-promoting potentials stored in both sweet and tart varieties. This avenue of research is all the more important as Americans increasingly look to the foods they eat for function as well as flavor. Along with an aging population and more focus on plant-based diets, this rapid shift of attention to the foods we eat aligns with many of the distinct benefits that sweet cherries offer, including those that may prevent – or reduce risk or severity of – several chronic inflammatory diseases and other conditions.

Beyond the eponymous red color and well-loved flavor of sweet cherries, they tout high concentrations of a number of studied phytonutrients, including anthocyanins. It's these anthocyanins that give cherries their deep, vibrant color and help deliver powerful antioxidant and anti-inflammatory benefits. The increasing number of studies available provide an evermore detailed map of the breadth of their benefits, including those that directly measure the effects of sweet cherry consumption across various biomarkers for human diseases and conditions.

Initial research results suggest that eating sweet cherries can have a beneficial effect on inflammation, arthritis, blood pressure, cancer, cardiovascular disease, diabetes, cognitive function, sleep and stress. Consider reviewing the work of Dr. Darshan Kelley, a leader in conducting human interventional studies with sweet cherries and in uncovering potential benefits across multiple biomarkers. Another researcher, Dr. Giuliana Noratto, recently added to the body of work on sweet cherries with compelling new evidence of their beneficial effects on breast cancer, the gut microbiome and intestinal health. For over 70 years, our self-funded organization



of the now 2,100 cherry growers from across five Northwest states has worked to learn all we can about the sweet cherries we grow and how to grow them better. For almost 20 years, this has included health research into a number of sweet cherry varieties. We recognize and embrace the need for continued research,

particularly long-term human studies, and value the investigative opportunities we've funded at the USDA-ARS Western Human Nutrition Research Center and Texas A&M University.

Although we are only beginning to understand the full value of sweet cherries, we are pleased to share our findings to date. Please read on for emerging thought on the wellness benefits of sweet cherries. We hope you incorporate this research as you build nutrient-dense, plant-based diets, and consider sharing the advantages of sweet cherries with colleagues and clients.

Sincerely,

James Michael

VICE PRESIDENT OF MARKETING – NORTH AMERICA
NORTHWEST CHERRY GROWERS



For information about grower-funded research opportunities, please contact James at james@nwcherries.com or 509.453.4837.

1 *Keep pain at bay with anti-inflammatory properties*

Sweet cherries contain anthocyanins, which appear to shut down enzymes that cause tissue inflammation in a similar manner to ibuprofen and naproxen. Increased inflammation is the underlying cause for numerous chronic human diseases, such as:

- Arthritis • Diabetes • Cancer • Hypertension
- Cardiovascular disease

Biomarkers of these diseases and C-reactive protein, a common marker of inflammation, have been reduced in human studies of cherry consumption.

2 *A tastier way to fight cancer*

More research is suggesting that sweet cherries may possess cancer-fighting properties. Among other compounds, cherries contain ellagic acid and anthocyanins, which appear to be potent inhibitors to the growth of cancer cells. Along with other phytonutrients, their individual and synergistic benefits are the focus of several new studies.

3 *Take the bite out of gout attacks*

A painful form of arthritis caused by elevated levels of uric acid in the blood, gout affects more than 8.3 million Americans. Eating sweet cherries can lower the levels of uric acid in the blood, according to research conducted at the USDA Western Human Nutrition Research Center. A study done at the Boston University School of Medicine reports patients who eat cherries and take their medicine have a 35% to 75% lower chance of experiencing an attack.

Cherry Benefits Better Health



6— y-licious efits for ter! alth-

4

*Sweet cherries,
sweeter dreams*

One of the few plant sources of melatonin, sweet cherries are a natural and flavorful aid in improving the quality of sleep. Eating cherries about an hour before bedtime may help stabilize and regulate sleep patterns.

5

*Snack on a sweet
source of fiber*

A cup of sweet cherries delivers about three grams of fiber, or about 12% of the daily value from USDA Dietary Guidelines. Just two cups of fruit daily can contribute to healthy weight maintenance, diabetes prevention and improved cardiovascular health.

6

*A sweet fix without
busting GI levels*

Satisfy a sweet tooth without worry. Cherries boast a lower glycemic index than almost any other fruit. They release glucose slowly and evenly, so blood sugar levels stay steady longer.



Studies Show...

Sweet cherries are a flavorful source of potassium¹ as well as important nutritional properties and bioactive compounds, including:

- *Polyphenolics: anthocyanins, flavonoids, hydroxycinnamic acids*
- *Indolamines: tryptophan, melatonin, serotonin*

These compounds, gained through consuming dark sweet cherries, contribute to a host of beneficial effects on certain diseases and conditions.

BLOOD PRESSURE

- Hypertension is a risk factor in cardiovascular disease, and studies suggest phenolic acids found in cherries and produced by anthocyanin metabolism exert vasorelaxing and antihypertensive effects.²

CANCER

- In lab studies, the phenolic compounds of sweet cherries appear to inhibit breast cancer cell growth without toxicity to normal cells.³
- Sweet cherry extracts have been shown to inhibit proliferation of colon and breast cancer cells in several published studies.⁴
- Sweet cherries contain perillyl alcohol – shown to be capable of inhibiting pancreatic, breast, liver, colon, skin and lung cancers – which raises the fruit's anti-carcinogenic activity.⁵

CARDIOVASCULAR DISEASE (CVD)

- Anthocyanins found in foods like sweet cherries inhibit lipid peroxidation, which has a hand in reducing CVD risk factors.⁶
- Anthocyanin interference with inflammation pathways can help in prevention of CVD.⁷

¹ "Sweet and sour cherries: Origin, distribution, nutritional composition and health benefits." Federica Blando and B. Dave Oomah. *Trends in Food Science & Technology* 86 (2019) 517-529.

² Blando, et al.

³ "Dark sweet cherry (*Prunus avium* L.) phenolics as dietary chemopreventive/therapeutic compounds for aggressive breast cancer cell growth with no toxicity to normal breast cells." Layosa MA, Lage NN, Martens-Talcott SU, Talcott St, Pedrosa ML, Chew BP and Noratto GD.

⁴ "Nutrients, Bioactive Compounds and Bioactivity: The Health Benefits of Sweet Cherries." Ana C. Gonçalves, Catarina Bento, Branca Silva, Manuel Simões, Luís R. Silva. *Current Nutrition & Food Science*, 2019 15, 208-227.

⁵ Gonçalves, et al.

⁶ Blando, et al.

⁷ Blando, et al.

⁸ Blando, et al.

⁹ Blando, et al.



COGNITIVE FUNCTION

- Improved brain and visual function may result from anthocyanin's interference in inflammation pathways.⁸
- Anthocyanins appear to exert neuroprotection, resulting in a beneficial effect on cognitive decline and neurodegeneration associated with aging.⁹
- Consumption of anthocyanins from cherries appears to improve memory and cognition in older adults with mild-to-moderate dementia.¹⁰

DIABETES

- The polyphenols in cherries appear to help diminish hyperglycaemia, oxidative stress and inflammatory markers that are predictors of diabetes mellitus.¹¹
- Cherry extracts reduce glucose blood levels and protect pancreatic beta-cells from oxidative damage, enabling them to continue balanced production of insulin.¹²

GOUT

- Consumption of cherries can significantly decrease plasma urate, which provides anti-gout efficacy.¹³
- Phenolics appear to interfere with the oxidative process as free radical terminators, ultimately decreasing formation of volatile decomposition products that contribute to gout.¹⁴
- Sweet cherries compared favorably to NSAID controls using ibuprofen and naproxen to alleviate gout symptoms.¹⁵

¹⁰ "Acute reduction in blood pressure following consumption of anthocyanin-rich cherry juice may be dose-interval dependant: a pilot cross-over study." Katherine Kent, Karen E. Charlton, Andrew Jenner and Steven Roodenrys. *International Journal of Food Sciences and Nutrition*, 2016, 67:1, 47-52.

¹¹ Gonçalves, et al.

¹² Gonçalves, et al.

¹³ Blando, et al.

¹⁴ "Is there a role for cherries in the management of gout?" Marcum W. Collins Kenneth G. Saag, Jasvinder A. Singh. *Therapeutic Advances in Musculoskeletal Disease*, 2019, Vol. 11: 1-16.

¹⁵ Collins, et al.

¹⁶ "Consumption of 'Bing' sweet cherries lowers circulating concentrations of inflammation markers in healthy men and women." Kelley, D. S., Rasooly, R., Jacob, R. A., Kader, A. A. & Mackey, B. M. *Journal of Nutrition*, 2006, 136, 981-986.

INFLAMMATION

- Eating cherries significantly decreased C-reactive protein and nitrous oxide concentrations, both known pro-inflammatory factors.¹⁶
- Consuming cherries was found to decrease plasma concentrations of eight biomarkers associated with inflammatory diseases (CRP, ferritin, IL-18, TNFα, IL-1Ra, ET-1, EN-RAGE and PAI-1).¹⁷
- Polyphenols in cherries may minimize or prevent inflammation and oxidative stress, which may be risk factors for diseases like arthritis, diabetes, cancer and hypertension.¹⁸

SLEEP

- The presence of tryptophan, serotonin and melatonin in sweet cherries interact with cherry phenolics to help regulate sleep cycles.¹⁹

STRESS

- Cherry phenolics appear to protect neuronal cells from cell-damaging oxidative stress.²⁰
- Various studies have shown serotonin is an important neurotransmitter that reduces stress and improves mood.²¹

¹⁷ "Sweet Bing Cherries Lower Circulating Concentrations of Markers for Chronic Inflammatory Diseases in Healthy Humans." Darshan S. Kelley, Yuriko Adkins, Aurosis Reddy, Leslie R. Woodhouse, Bruce E. Mackey and Kent L. Erickson. *The Journal of Nutrition*, American Society of Nutrition, 2013, doi: 10.3845/jn.112.171371.

¹⁸ Kelley, et al., 2013.

¹⁹ Gonçalves, et al.

²⁰ Blando, et al.

²¹ "The consumption of a Jerte Valley cherry product in humans enhances mood, and increases 5-hydroxyindoleacetic acid but reduces cortisol levels in urine." María Garrido, Javier Espino, David González-Gómez, Mercedes Lozano, Carmen Barriga, Sergio D. Paredes, Ana B. Rodríguez. *Experimental Gerontology*, 2012, 47, 573-580.



DARSHAN S. KELLEY, PH.D.



Dr. Kelley has been interested in the effects of dietary factors on oxidative stress, inflammation and immune responses for nearly four decades. He dedicated 35 years to the Agricultural Research Service of the USDA in its only lab devoted to human nutrition in the western U.S., the Western Human Nutrition Research Center in California. He spearheaded studies as lead scientist or research leader for more than 25 years, earning recognition for breakthrough findings on the impacts of diet on human health. Additionally, Dr. Kelley was an adjunct professor in the Department of Nutrition at the University of California Davis and served as the major professor for PhD and MSc students. He has served on the editorial boards for several nutrition journals, advisory boards of Washington State Fruit Commission and California Cherries.

The focus of Dr. Kelley's research has been the modulation of risk factors for cardiovascular disease, insulin resistance, diabetes, non-alcoholic fatty liver disease and cancer by individual dietary factors. He was among the first to conduct human interventional studies with sweet cherries and was the first to describe the anti-inflammatory effects of cherries in human subjects.

Increased inflammation is a major contributing factor to the development and harmful outcomes of human chronic inflammatory diseases such as diabetes, cardiovascular disease and cancer. Results of Dr. Kelley's numerous studies show that diet is a major reason for the increased incidence of these inflammatory diseases; their incidence can be lowered, in part, by increasing the consumption of foods rich in polyphenols.

Dr. Kelley is the founder and CEO of Kelley Nutraceuticals and is a member of the American Society for Nutritional Sciences, the International Scientific Society for Fatty Acids and Lipids, and the British Nutrition Society. He is a past recipient of the Robert H. Herman Award for Clinical Nutrition from the American Society for Nutrition, and he was recognized with the Best Paper Presentation Award at the 10th International Congress of Immunology. He completed his undergraduate work and his Master of Science in biochemistry at Punjab Agricultural University in India, his doctorate at Oklahoma University in Oklahoma City, and his post-doctorate work in cancer research at McArdle Laboratory for Cancer Research, University of Wisconsin, Madison.



GIULIANA NORATTO, PH.D.



Dr. Giuliana Noratto, an assistant research professor at Texas A&M University, Nutrition and Food Science Department, is a member of the American Society of Nutrition and the Society of Toxicology. Dr. Noratto's research with dark sweet cherries, funded by the Northwest Cherry Growers, has resulted in scientific peer-reviewed publications disclosing the mechanisms by which cherry bioactive compounds are able to modulate the intestinal bacteria to shift host physiology and delay or prevent the onset of diseases linked to obesity, such as diabetes, liver disease and heart disease. In addition, Dr. Noratto has been investigating the anti-breast cancer activity of polyphenols extracted from dark sweet cherries using *in vitro* and *in vivo* animal research models. This research has revealed the molecular mechanisms modulated by dark sweet cherry polyphenols that delay breast

tumor growth and the enhanced anti-cancer activity of dark sweet cherry anthocyanins which target multiple molecular pathways.

A recipient of the American Society of Nutrition 2015 Mary Swartz Rose Young Investigator Award, Dr. Noratto focuses her research on phytochemicals and other bioactive compounds including dietary fiber extracted from fruits and vegetables and their role in the prevention of obesity-related chronic diseases. Research projects look to integrate microbiome, metabolomics and proteomics analyses to investigate the biological mechanisms influenced by dietary interventions and their correlations with end point biomarkers of obesity-related diseases including diabetes, cancer and cardiovascular disease.





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