

**CALIFORNIA CHERRY BOARD AND WASHINGTON STATE FRUIT COMMISSION
HEALTH AND NUTRITION COMMITTEE MEETING NOTES**

**Scientific Advisory Board Meeting
March 22, 2018 – Suncadia Resort, Cle Elum, WA**

- I. Meeting called to order at 3:00
- II. Participants:
 - Ed Clark (WSFC, Board Member)
 - Jim Kelley (WSFC, Board Member)
 - Norm Gutzwiler (WSFC, Board Member)
 - Tom Gotelli (O-G Packing, California)
 - Darshan Kelley, Ph.D., Western Human Nutrition Research Center
 - Kevin Laugero, Ph.D., Western Human Nutrition Research Center
 - Giuliana Noratto, Ph.D., Texas A&M University
 - Chris Zanobini (CCB)
 - Tyler Rood (CCB)
 - B.J. Thurby (WSFC)
 - James Michael (WSFC)
 - Teresa Baggarley (WSFC)
 - Eric Rosenberg (BCI)
 - Alissa Chevallier (BCI)
- III. Comments by B.J. Thurby
 - a. Emphasized the importance of developing a global message on cherry health benefits. Industry agrees that this is highly important and that resources should continue to be devoted to research, and that global partnerships in the cherry industry should be pursued. Jim Kelley highlighted the importance of high-quality research in order to make claims that have a solid scientific basis.
- IV. Discussion of state of the growing season, California and Washington
 - a. California saw a mild winter through December, and then colder weather since.
 - b. Washington: TriCities and Chelan likely to be a few days earlier than last year. Big spread between regions this year. Seeing fewer cherries per bud (~2/bud vs. 4-5/bud last year).
- V. Presentation by James Michael on services provided by LANE, a Finn Partners Company
 - a. Marketing services firm focused on health, wellness, and food/beverage, based in Portland, OR.
 - b. Development of marketing materials based on cherry health attributes as determined through research program.
 - c. WSFC 2017 Health Campaign garnered 967.4 million media impressions around the positive health attributes of NW sweet cherries
- VI. Presentation by Darshan Kelley, PhD. Research Chemist, ARS, USDA Western Human Nutrition Research Center: “A Review of Health Benefits of Cherries.”
 - a. This presentation is based on a review article to be published online in the journal “Nutrients” next week.
 - b. First cherry health research in 1950 by L.W. Blau on gout, saw significant improvement but the results were not widely known.
 - c. Cherry composition

- i. Contains fiber, polyphenols, carotenoids, vitamin C, potassium, tryptophan, serotonin, and melatonin (could these last three have cognitive effects on behavior and sleep?)
 - ii. Sweet cherries have fewer polyphenols overall than tart cherries, but sweet have 50-100% more anthocyanins, which are the compounds believed to have most significant effect on oxidative stress and inflammation.
 - iii. Anthocyanin content varies greatly by variety, growing conditions, harvest conditions, etc.
 - iv. While previously believed that anthocyanins were at peak concentration in the blood 2 hours after consumption, recent research suggests that peak concentration is at 10 hours post-consumption, with detectable quantities remaining for up to 48 hours.
- d. Next studies not done until early 2000s (Jacob, Kelley, Connolly), also showed encouraging results (oxidative stress, inflammation). Dr. Kelley's first study, with funding from CCB and WSFC, was begun in 2006, and samples collected for that study were analyzed further for a second publication in 2013.
 - i. 2006 Aims: Determine effects of cherry consumption on inflammation, blood lipids, insulin resistance.
 - ii. Used fresh cherries from Lodi, collected weekly and stored under CO₂.
 - iii. Found significant decreases in markers of inflammation.
- e. Kelley et al., 2013 study
 - i. Evaluated the plasma samples collected for the 2006 study for a wide range of biomarkers. Found changes in many markers for oxidative stress, inflammation, and chronic inflammatory diseases (arthritis, diabetes, cardiovascular disease, hypertension, cancer).
 - ii. To follow up, will need to conduct human studies to evaluate clinical end points for arthritis, diabetes, hypertension, and cardiovascular disease, as well as animal studies to determine cancer effects.
- f. For review article, 29 human cherry studies were analyzed and it was found that cherry products were effective in:
 - i. 8/10 studies on oxidative stress
 - ii. 11/16 studies on inflammation
 - iii. 8/9 studies on excise recovery
 - iv. 5/5 studies on arthritis
 - v. 4/4 studies on sleep
 - vi. 2 studies also evaluated effect on stress
 - vii. 9 studies evaluated effect on diabetes and cardiovascular disease
 - viii. Most of these studies were short-term, but still showed that cherries can be quite effective
 - ix. Effect of cherries on memory are significant and this will be a component of Dr. Laugero's upcoming research
- g. Questions/ Comments from the industry:
 - i. B.J. Thurlby: One of the major issues to discuss is that SAB has been working to develop an easy-to-dose product for use in these studies.
 - ii. There are certain problems with frozen cherries, as these tend to be the last ones off the line and may sit in packing shed before being frozen, which could compromise polyphenol/anthocyanin content. To be used for research, cherries would need to be put straight into cold room and then to

flash freezer. The powder that was developed previously turned out to have very low anthocyanin content, but it is unclear whether this depletion occurred in the cherries themselves, during storage of cherries, during powder production, or during powder storage.

- iii. Dr. Noratto suggested that the de-pitting process could play a role in anthocyanin oxidation, as this process releases enzymes that can oxidize these compounds. She pointed out that Powder Pure's process did not involve a blanching step to de-activate such enzymes. It was suggested that freeze-drying may actually be more effective than Powder Pure's proprietary process.

VII. Presentation by Kevin Laugero, PhD. Scientist, ARS, USDA Western Human Nutrition Research Center: "An Overview of a Proposed Clinical Trial to Test Cardiometabolic Health Benefits of Sweet Cherry Consumption."

- a. There are six federally-funded nutrition centers in the U.S., WHNRC's mission is to "Improve dietary recommendations by understanding variability in peoples' responses to diets, nutrients, and other food constituents."
- b. Dr. Laugero's laboratory is the Stress Biology and Nutrition Research lab, proposes to look at the effect of cherries reducing risk factors for metabolic syndrome, and whether cherries can disrupt stress' known role in metabolic syndrome.
 - i. Risk factors for Metabolic Syndrome: visceral obesity, insulin resistance, low-HDL-cholesterol, high triglycerides, hypertension.
 - ii. Many prior studies have looked only at healthy adults and have not included a placebo. Alternatively, many studies only looked at these risk factors as a secondary outcome of their study, which is known to influence the results.
 - iii. Need for placebo-controlled studies of sweet cherry effects on cardiometabolic risk factors. Also need a form of cherry that extends availability throughout the year and provides a consistent dose of cherry compounds (Juice? Concentrate? Powder?)
 - iv. According to 6 studies, cherries may have protective effects against stress, which is linked to metabolic syndrome.
- c. Two primary research questions:
 - i. Does cherry powder (or other substance) consumption lower risk for cardiometabolic disease in a placebo-controlled study?
 - ii. Are these effects mediated through changes in brain stress pathways?
- d. Study design:
 - i. 30-75-year-old men and post-menopausal women, prehypertensive, overweight or moderately obese.
 - ii. Four servings of cherries per day for two consecutive six-week periods.
 - iii. Crossover design – placebo group and cherry group will be switched in the middle of study.
 - iv. Two types of test visits with 3-5 days between visits.
 - v. Tests include blood pressure, vascular tone, inflammatory and metabolic responses, oral glucose tolerance test (for insulin resistance), stress test.
 - vi. Stress test component will increase the signal-to-noise and allow for determination of whether cherry consumption blunts the stress response known to play a role in metabolic syndrome
- e. Project update:
 - i. USDA/ARS contracts office is finalizing agreement.

- ii. Human Studies Committee has approved the study.
- iii. Cherry powder analysis showed that the powder is depleted in anthocyanins – need to find an alternative source of cherry.
- iv. Frozen cherry analysis is in progress.
- f. Questions/ Comments from the industry:
 - i. Tom Gotelli: Would it be possible to include cognitive function testing? This is not something that was initially part of the proposal but could easily be added. Industry would like to see this added, if possible, as the results on memory/cognitive function that Dr. Kelley presented appear to be quite promising. This could be an important claim that may encourage consumers to think about the more immediate health effects of consuming cherries. Results showing a cognitive effect would be particularly exciting as there are no good pharmaceuticals available to improve cognition. Dr. Laugero estimates that adding cognitive function testing would add only a few thousand dollars to the total study cost, as the main expense is the purchase of licenses to use the cognitive testing software.
 - ii. Jim Kelley inquired about whether it would be possible to pursue opportunities for collaboration with the pharmaceutical industry in the future. Dr. Noratto reported that the pharmaceutical industry is increasingly looking for ways to use nutritional products to enhance their own compounds, and so such opportunities are certainly out there.
- VIII. Presentation by Giuliana Noratto, PhD., Research Assistant Professor, Texas A&M University: “Prevention of obesity-related disease through cherry consumption: What can we say so far?”
 - a. Cherries and intestinal health
 - i. Obese individuals are known to have a different composition of gut microbiota than non-obese individuals. Notably, obese gut microbiota are characterized by large numbers of “Proteobacteria,” a phylum containing a variety of pathogenic bacteria.
 - ii. Hypothesis: As cherries are a good source of insoluble fiber, they are expected to alter the composition of gut microbiota in obese mice.
 - iii. After 12 weeks, cherry consumption altered microbiota, in particular reducing the proteobacteria by more than 50% and increasing the population of verrucomicrobia (a group that includes *A. muciniphila*, which is believed to decrease intestinal inflammation) to levels higher than the control group.
 - iv. Increased production of short chain fatty acids in cherry group, which are important in maintaining healthy gut barrier function and reducing the risk of inflammatory disease. Thickness of the colon wall was also visibly increased, though the results were not statistically significant.
 - v. Future studies: since the mice used in this study were genetically-engineered to be obese, this model does not take into account possible anti-inflammatory effects of cherries. Might see a greater effect on biomarkers in a high sugar/fat diet-induced obesity model.
 - vi. Paper published January 2018.
 - b. Cherries and the prevention and treatment of diabetes and non-alcoholic liver disease (NALD)
 - i. Obesity and type-2 diabetes increase risk of NALD, one of the most common liver diseases in the world.

- ii. When she did not find the published effects, Dr. Noratto analyzed the cherry powder and found that it was very low in anthocyanins. Therefore, this study instead looks at the effect of non-anthocyanin polyphenols on NALD.
 - iii. This anthocyanin-depleted cherry powder improved some of the blood biomarkers of inflammation and diabetes (IL-6, hepatic steatosis, insulin sensitivity, inflammation).
 - c. Cherries and the prevention and treatment of breast cancer
 - i. Obesity increases the risk of post-menopausal breast cancer
 - ii. First step was an *in vitro* study to determine which types of breast cancer would be most responsive to cherry compounds. Found that HR-/HER2+, the most aggressive form of breast cancer, is also the most responsive to cherry extract. The whole extract was most effective, but also found that procyanidins and anthocyanins have similar effectiveness.
 - 1. Cherry juice concentrate (stabilized, with sugar removed) is being used for this study.
 - iii. The lab is currently engaged in ongoing studies to elucidate the molecular mechanism for this anti-cancerous effect.
 - iv. Also have an ongoing *in vivo* study (mice). Only preliminary results available, but the tumors in mice given cherry extract appear to be growing slower than the control group. Will need at least four more weeks of data before conclusions can be drawn.
 - v. Next step would be to evaluate effects on metastasis. Dr. Noratto has experience with such studies in peaches.
 - vi. Another year of funding remains for this study.
 - d. Questions/ Comments from the industry:
 - i. There was much enthusiasm from the industry regarding these results, particularly of the breast cancer study. The group looks forward to seeing the results of the *in vivo* study and then evaluating what would be the next best steps to pursue.

IX. Meeting Wrap-up