P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

HerbClip™

File: ■ Blackcurrant (*Ribes nigrum*, Grossulariaceae)
■ Anthocyanins
■ Parkinson's Disease

HC 081854-613

Date: March 29, 2019

RE: Blackcurrant Increases Cyclic Glycine-proline in Cerebrospinal Fluid and Has Potential to Treat Parkinson's Disease

Fan D, Alamri Y, Liu K, et al. Supplementation of blackcurrant anthocyanins increased cyclic glycine-proline in the cerebrospinal fluid of Parkinson patients: Potential treatment to improve insulin-like growth factor-1 function. *Nutrients*. June 2018;10(6):714. doi:10.3390/nu10060714.

Insulin-like growth factor-1 (IGF-1) is a neurotrophic factor, which is involved in neuronal survival and brain function. However, in patients with Parkinson's disease (PD), there is an increase in circulating IGF-1 and impaired IGF-1 function. This impaired function is thought to contribute to disease progression. Changes in plasma IGF-1 may predict prognosis and treatment responses in PD. However, most of the measurable plasma IGF-1 is inactive because it is bound to IGF binding protein (IGFBP), in particular, IGFBP-3. Therefore, plasma IGF-1 concentration does not represent the function of IGF-1. Cyclic glycine-proline (cGP) is a metabolite of free (i.e., not bound to IGFBP) bioactive IGF-1. cGP can also bind to IGFBP-3. When cGP binds to IGFBP-3, there is more free, bioactive IGF-1. Thus, cGP levels are a marker for free bioactive IGF-1. In vivo studies indicate that blackcurrant (*Ribes nigrum*, Grossulariaceae) anthocyanins (BCA) may alter the IGF-1 pathway. Further, high consumption of anthocyanins from berries are associated with a lower risk of PD. Thus, the purpose of this open-label study was to evaluate the effect of BCA on IGF-1 function.

Men (n = 11, aged ≥ 40 years) with PD confirmed by a movement disorders neurologist were recruited from the Van der Veer Movement Disorders clinic and the patient database of New Zealand Brain Research Institute, Christchurch, New Zealand. Included patients had any stage and duration of PD. At the first visit (baseline), patients underwent the following battery of tests: Unified PD Rating Scale (UPDRS) part III, the Hospital-associated Anxiety and Depression Scale (HADS), the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the PD Questionnaire (PDQ-39). To avoid learning effects, different versions of the tests were used for the second visit if available. Then plasma and cerebral spinal fluid (CSF) samples were collected. All patients were treated with 300 mg twice daily of BCA concentrate (35% anthocyanins, Super Currantex 20, supplied by Vitality New Zealand,

manufactured by Just the Berries Ltd.; Christchurch, New Zealand) for four weeks. Patients were instructed to consume a "low-anthocyanin diet" (i.e., white rice [*Oryza sativa*, Poaceae], white bread, tuna, chicken, coffee [*Coffea* spp., Rubiaceae], and non-herbal tea [*Camellia sinensis*, Theaceae]) 12 hours before visit 1 and visit 2. The last dose of BCA was taken during or just before visit 2. At visit 2, plasma and CSF samples were collected. Concentrations of cGP, IGF-1, and IGFBP-3 were measured in the plasma and CSF with enzyme-linked immunosorbent assay (ELISA) and high performance liquid chromatography mass spectrometry (HPLC-MS) assay. An in vitro analysis was also conducted to assess the level of cGP in BCA.

The majority of patients were diagnosed as having idiopathic PD without obvious cognitive impairment. The in vitro analysis demonstrated that there was a dose-dependent increase in cGP concentration with an increased dose of BCA ($P < 0.0001$). There was a mean 74.4% increase in cGP concentration in CSF after patients were treated with BCA ($P < 0.05$). However, there was high patient variability in the rate of increase of cGP in CSF. The change in cGP in the CSF was not accompanied by a change in plasma cGP. There were no significant changes in the CSF or plasma concentrations of IGF-1, cGP/IGF-1 ratio, and IGFBP-3. However, there was a strong positive correlation between each patient's cGP concentration in the CSF and in the plasma, indicating that plasma cGP may be the source of the CSF cGP.

The BCA-induced increase in CSF cGP concentrations indicates that BCA has oral bioavailability and can lead to brain uptake of cGP. The authors state that "The data provide the first clinical evidence for oral availability and effective central uptake of cGP following the intake of foods." The increase in CSF cGP could lead to improved IGF-1 function in the brains of patients with PD. However, this hypothesis needs to be further tested. Preliminary clinical trial results of BCA have been inconclusive. It should be noted that the results from this study are limited by the small population size and the large interpatient variability.

The authors declare no conflict of interest. The study was funded by Vitality New Zealand, New Zealand Brain Research Institute, and University of Auckland, New Zealand.

—Heather S. Oliff, PhD

Referenced article can be accessed at https://www.mdpi.com/2072-6643/10/6/714.