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**File: ■ Coffee (*Coffea arabica*)
■ Neurotrophins
■ Exosomes**

HC 101351-483

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RE: Whole Coffee Fruit Concentrate Increases Acute Blood Levels of Brain-derived Neurotrophic Factor

Reyes-Izquierdo T, Argumedo R, Shu C, Nemzer B, Pietrkowski Z. Stimulatory effect of whole coffee fruit concentrate powder on plasma levels of total and exosomal brain-derived neurotrophic factor in healthy subjects: an acute within-subject clinical study. *Food Nutr Sci.* 2013;4:984-990.

Brain-derived neurotrophic factor (BDNF) is a growth factor that regulates several activities of the central nervous system. For example, it promotes neuron survival and influences mood, sleep, and appetite. As the body grows older, BDNF levels decrease. The decrease is associated with depression and brain aging. BDNF is able to circulate in the blood. Exosomes are vesicles that contain molecular constituents from their cell origin such as proteins and RNA. Exosomes travel and merge with other cells, thereby, passing on the contents and providing cell-to-cell signalling, even crossing the blood-brain barrier. Exosomes from various types of blood cells may carry BDNF. A pilot study demonstrated that a single dose of whole coffee (*Coffea arabica*) fruit concentrate powder significantly increased plasma levels of BDNF.¹ The purpose of this single-blind, placebo-controlled, crossover study was to confirm and extend the findings of the pilot study.

Healthy subjects (n = 20) aged 25-35 years, with body mass index between 18.5 and 24.9 kg/m² and who did not use any type of medication or supplement for a period of 15 days prior to the start of the study were included. Also, at the time of the study, included subjects had to be free of rhinitis, influenza, and any other symptoms of upper respiratory infection. Subjects were excluded if they had diabetes mellitus, a known allergy to any of the test ingredients, or were using any anti-inflammatory, analgesic, anti-allergy, antidepressant medication, or multivitamins. The study was conducted in Guadalajara, Mexico. Subjects were treated with placebo on Day 1, 100 mg whole coffee fruit concentrate (FutureCeuticals, Inc.; Momence, Illinois) on Day 2, and 300 mL of freshly brewed coffee on Day 3. The brewed coffee was from San Francisco Bay Coffee One Cup for Keurig K-Cup Brewers, French Roast (San Francisco, California), which contains 130 ± 10 mg of caffeine. Blood was collected at baseline, 60 minutes,

and 120 minutes after treatment each day. Subjects fasted for 12 h prior to the first blood collection.

Whole coffee fruit concentrate significantly increased BDNF by 91% at 60 minutes and 66% at 120 minutes compared to baseline ($P < 0.001$). This increase was significantly greater than placebo at 60 minutes ($P = 0.0073$), and significantly greater than brewed coffee at 60 min ($P = 0.02$) and 120 min ($P = 0.04$). The brewed coffee did not significantly increase BDNF levels compared with placebo. One subject received an additional dose of coffee fruit concentrate to evaluate exosomal BDNF. Serum BDNF increased over baseline by 54% and exosomal BDNF by 206% after 60 minutes, decreasing to 32% and 39% increases, respectively, after 120 minutes.

The authors hypothesize that since whole coffee fruit concentrate does not contain BDNF, the whole coffee fruit concentrate could be stimulating release of endogenous BDNF from cells and from exosomes derived from blood cells. The hypothesis of the release of exosomal BDNF needs to be validated since the data were only from 1 subject. It should be noted that this study was conducted in healthy subjects, and the results may vary in other populations. These findings confirm the authors' pilot data. However, the sample size was small. The authors do not describe how the chemical composition of this patented extract of whole coffee fruit differs from the chemical composition of brewed coffee. It is unclear if the effect is concentration-dependent or something else. For example, could a more concentrated brewed coffee produce a similar effect? The potential for influencing the effects of aging and chronic neurodegenerative diseases makes further characterization and study of this preparation intriguing.

—Heather S. Oliff, PhD

Reference

¹Schulman R. Levels of a brain protein involved in cognition increased with whole coffee fruit concentrate powder supplementation. *HerbClip*. May 31, 2013 (No. 021324-473). Austin, TX: American Botanical Council. Review of Modulatory effect of coffee fruit extract on plasma levels of brain-derived neurotrophic factor in healthy subjects by Reyes-Izquierdo T, Nemzer B, Shu C, et al. *Br J Nutr*. 2013;110(3):420-425.

Referenced article can be found at www.scirp.org/journal/PaperDownload.aspx?paperID=36447.

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