Title – Pheophorbide Esters A and B Isolated from Acai Berries as Activators of Apoptosis

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Mentor(s) and Mentor Email - Dr. Gregory Raner (graner@liberty.edu)

Student name(s) and email(s) – Thomas Siff (tsiff@liberty.edu)

Abstract: In the last decade, the use of natural products for health supplementation has increased beyond the ability of researchers to fully analyze all of the products being consumed by the public. One of the most popular natural products currently on the market is the Brazilian acai berry (*Euterapia oleracea*), a small purple berry with strong antioxidant properties known to aid in weight loss, lowering cholesterol levels, and reducing high blood pressure. While such effects are certainly beneficial, it is not yet known which compounds in the acai berry are responsible for them or the mechanism by which they act. Previous research has identified pheophorbide esters A and B as potent activators of the cellular antioxidant response via activation of Nrf2, the master regulator of the antioxidant response. The antioxidant response is initiated in response to increased levels of harmful reactive oxygen species, which if left unchecked, leads to cell death by apoptosis. We therefore hypothesized that pheophorbide esters A and B would activate apoptosis in human liver cells. To test this hypothesis, HepG2 human hepatocarcinoma cells were treated with different concentrations of both pheophorbide esters and brusatol, a well-characterized anticancer drug and apoptosis inducer. The resulting effects were measured using a commercial fluorescence assay that detects levels of caspase-3, a key mediator of apoptosis. Brusatol treatment resulted in a dose-dependent increase in caspase-3 activation, while pheophorbide treatment showed little activation below 20 mg/mL. Thus, it appears that the pheophorbide esters increase cellular oxidative stress slowly enough to be harmful only at high concentrations, unlike the harmful effects of brusatol at any dosage. This suggests that the pheophorbide esters could act as sensitizers to apoptosis, helping to
preemptively remove damaged and cancerous cells from the body. Further research will focus on quantifying the time- and dose-dependent effects of these compounds.