

Effect of Dried Plum and Blueberry Extracts on Inflammatory Gene Expression

According to the Alzheimer's Association, an ~5.1 million Americans age 65 and older have the neurodegenerative disease Alzheimer's Disease (AD). The number of cases is projected to increase 40% by 2025. Of the top 10 causes of death in the U.S. (and the 6th leading cause of death in Oklahoma), AD is among the few diseases for which there are few treatment options that exhibit only limited effectiveness. However, large scale studies indicate that diets rich in fruits and vegetables are associated with a

reduced risk of developing and delaying AD onset. Recent research indicates that inflammation of the CNS contributes to the development of AD (Morales et al., 2014). Microglial cells, specialized macrophages in the CNS, play a crucial role in inflammatory processes during disease advancement through the production of proinflammatory cytokines (Figure 1). Using the BV2 microglial cell line, researchers have shown that blueberry extracts can reduce inflammation in response to lipopolysaccharide (LPS), though the bioactive components responsible for these effects remain unknown (Xie et al., 2011). Compared to blueberries (BB), dried plum (DP) can reduce inflammation-induced bone loss and possesses higher levels of antioxidant compounds that may be more effective at reducing microglial inflammation (Rendina et al, 2013).

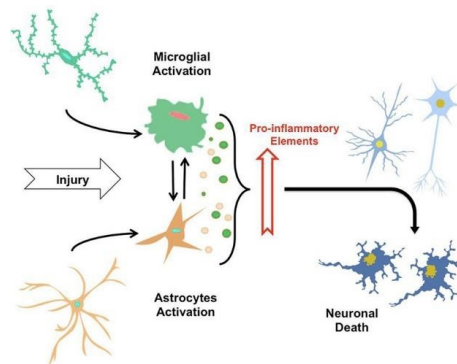


Figure 1. Role of microglial cells in neurodegeneration (Morales et al., 2014).

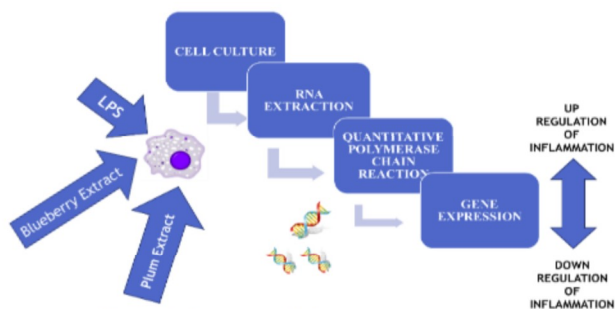


Figure 2. Experimental design

My **research question** is: can DP extracts reduce inflammation in BV2 cells, and if so, are they more effective than BB extracts? The **objective** of this study is to determine if these extracts reduce inflammatory gene expression in activated BV2 cells. BV2 cells will be grown and plated, and incubated for 24 hours at 37°C. Next, cells will be treated with each extract (6 µg/mL) ± LPS for 18 hr. The control will consist of cells treated with the solvent used to prepare the extracts. After 18 hr, total RNA will be extracted. The concentration and integrity of RNA will be

determined by spectrophotometry and gel-electrophoresis. RNA of appropriate quality will be used to synthesize cDNA for the analysis of gene expression. Next, quantitative real-time PCR (qPCR) will be performed to examine proinflammatory gene expression. These experiments will be repeated at least 3 times to ensure consistency of experimental results. I predict that compared to the control or BB extract, treatment of activated BV2 cells with DP will reduce inflammation. If these extracts reduce inflammation, it will provide further evidence that the incorporation of specific foods may be beneficial in reducing the risk of AD.

This study is important because chronic diseases such as AD are predicted to continue to increase over the next decade and have major impacts on families and overall healthcare costs. Incorporating specific foods into the diet is a cost-effective option for reducing the risk of AD and could also be used to diminish or slow the progression of the disease. Future studies could explore the impact of incorporating these extracts into the diet using animal models of neurodegenerative disease.

- Morales J, Guzmán-Martínez L, Cerda-Troncoso C, Fariás GA and Maccioni RB (2014) Neuroinflammation in the pathogenesis of Alzheimer's disease. A rational framework for the search of novel therapeutic approaches. *Front. Cell. Neurosci.* 8:112. doi: 10.3389/fncel.2014.00112
- Rendina, E., Hembree, K. D., Davis, M. R., Marlow, D., Clarke, S. L., Halloran, B. P., Smith, B. J. (2013). Dried Plum's Unique Capacity to Reverse Bone Loss and Alter Bone Metabolism in Postmenopausal Osteoporosis Model. *PLoS ONE*, 8(3), e60569. doi:10.1371/journal.pone.0060569
- Xie, C., Kang, J., Ferguson, M. E., Nagarajan, S., Badger, T. M. and Wu, X. (2011). Blueberries reduce pro-inflammatory cytokine TNF-α and IL-6 production in mouse macrophages by inhibiting NF-κB activation and the MAPK pathway. *Mol. Nutr. Food Res.*, 55: 1587–1591. doi: 10.1002/mnfr.201100344