## In vitro Study of Inflammatory Gene Expression Suppression of Strawberry and Blackberry Extracts

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Abstract: The physiology of various inflammatory diseases is a complex process mediated by inflammatory and immune cells such as macrophages and monocytes. Chronic inflammation, as observed in many cardiovascular and autoimmune disorders, occurs when the low-grade inflammatory response fails to resolve with time. Because of the complexity of the chronic inflammatory disease, major efforts have focused on identifying novel anti-inflammatory agents and dietary regimes that prevent the pro-inflammatory process at the early stage of gene expression of key pro-inflammatory mediators and cytokines. The ability of the extracts of three blackberry cultivars ('Jumbo', 'Black Satin' and 'Dirksen'), and one strawberry cultivar ('Camarosa') to inhibit four well-known genetic biomarkers of inflammation: inducible nitric oxide synthase (iNOS), cyclooxynase-2 (Cox-2), interleukin-1ß (IL-1ß) and interleukin-6 (IL-6) in an in vitro lipopolysaccharide-stimulated murine RAW 264.7 macrophage model were investigated. Moreover, the effect of latter extracts on the intracellular reactive oxygen species (ROS) and nitric oxide (NO) production was assessed. Assay was conducted with 50 µg/mL crude extract concentration, an amount that is easily achievable in the gastrointestinal tract after berries consumption. The mRNA expression levels of Cox-2 and IL-6 were reduced consistently (more than 30%) by extracts of 'Jumbo' and 'Black Satin' blackberries. Strawberry extracts showed high reduction in mRNA expression levels of IL-6 (more than 65%) and exhibited moderate reduction in mRNA expression of Cox-2 (more than 35%). The latter behavior mirrors the intracellular ROS production of the LPS stimulated RAW 264.7 macrophages after the treatment with blackberry 'Black Satin' and 'Jumbo', and strawberry 'Camarosa' extracts, suggesting that phytochemicals from these fruits may play a role in the health maintenance by reducing oxidative stress. On the other hand, effective inhibition in the gene expression of IL-1β and iNOS was not observed by any of blackberry and strawberry extracts. However, suppression in the NO production in the activated macrophages among 5-25% was observed by 'Jumbo' and 'Black Satin' blackberry extracts and 'Camarosa' strawberry extracts, suggesting a higher NO suppression property by phytochemicals of these fruits. All these results suggest the potential beneficial effects of studied berries as functional foods with antioxidant and anti-inflammatory roles. Moreover, the underlying role of phytochemicals from these fruits in the protection of inflammatory process will deserve to be further explored.

Keywords: cyclooxygenase-2, functional foods, interleukin-6, reactive oxygen species

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