Effects of Black Raspberry Extract

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Consumption of fruits and vegetables has been widely known to be able to prevent incidence of chronic diseases, such as cardiovascular diseases and dyslipidemia. Black rasbperry (BR) polyphenols, especially anthocyanins, have a variety of biological functions. The aims of this study were to investigate the effect of excessive choline intake on serum lipid profile and inflammation in rats fed high-fat diet and to evaluate the protective effect of polyphenols including anthocyanins in BR.

black raspberry polyphenols anthocyanins diet-induced hypercholesterolemia inflammation choline TMA TMAO

1. Introduction

Choline, one of the components of phospholipids in cell membrane and neurotransmitter, is regarded as an essential nutrient [1]. However, choline is also a precursor of trimethylamine-*N*-oxide (TMAO), which has been reported to act as a putative promoter of chronic diseases in human [2][3][4][5][6]. A part of excessive dietary choline is metabolized by gut microbiota to produce trimethylamine (TMA). Once TMA is absorbed from intestine, it is transported to liver via portal circulation and further oxidized to TMAO by hepatic flavin monooxygenases [2].

Since various epidemiological studies revealed connection between TMAO and cardiovascular diseases (CVD) [5][7][8], studies on TMAO and its precursors, such as choline, lecithin, and L-carnitine, have focused on vascular inflammation, endothelial dysfunction, and cholesterol homeostasis [3][4][5][9][10][11][12]. In addition, the effects of TMAO and its precursors on glucose intolerance [6] and hepatotoxicity [9][12] have been investigated. Taken together, it would likely be possible that TMAO can act in various organs throughout the body. More recently, TMAO has been demonstrated to induce expressions of cytokines and adhesion molecules in primary human aortic endothelial cells and vascular smooth muscle cells [3]. These inflammatory responses were also reported to be mediated via activation of nuclear factor-κB (NF-κB) signaling pathway, which is pivotal in inflammation, immunity, and cell death of various cell types [3].

Both epidemiological and experimental studies have revealed positive correlation between TMAO and chronic diseases such as CVD, renal disease, and diabetes [5][6][7][8][13][14][15][16]. Besides, evidences that TMAO might be able to cause hepatotoxicity or inflammation in adipose tissue have been provided [6][9][12]. However, consumption of fruits and vegetables has been widely known to be able to prevent incidence of chronic diseases.

Phytochemicals, bioactive compounds in plants, contribute to reduce risks of those diseases mostly by their anti-oxidant activity [17].

2. Black Raspberry (*Rubus occidentalis*; BR)

Black raspberry (*Rubus occidentalis*; BR) is relatively high in anthocyanins among *Rubus* fruits [18]. It has been found that the major bioactive compounds in BR were anthocyanins, mainly cyanidin-3-rutinoside (C3R), cyanidin-3-glucoside (C3G), and cyanidin-3-xylosylrutinoside (C3XR) [19][20]. BR has been known to possess anti-oxidative, anti-inflammatory, and anti-cancer activities [21]. Especially, C3R and C3G were demonstrated to have anti-inflammatory activity through down-regulating NF-κB expression and inhibiting inhibitory κB (I-κB) degradation in lipopolysaccharide (LPS)-treated murine macrophages [19]. However, to the best of our knowledge, protective effects of polyphenols in BR on inflammation induced by excessive choline intake have not been reported.

The aims of this study were to investigate the effect of excessive choline intake on serum lipid profile and inflammation in rats fed high-fat diet and to evaluate the protective effect of polyphenols including anthocyanins in BR.

3. Conclusions

Excessive choline can cause hypercholesterolemia and induce hepatic inflammation via, in part, NF-κB signaling pathway in rats fed high-fat diet. It might be due to elevated levels of cecal TMA and serum TMAO. Consistent intake of BR extract could lower the levels of cecal TMA and serum TMAO, which might result in the improvement of serum lipid profile in diet-induced hypercholesterolemia in rats. The result that BR could alter cecal TMA level suggests that BR polyphenols may act as a prebiotic in human gut as well. It could also alleviate hepatic inflammation via down-regulating the mRNA and protein expressions of genes related to inflammation. Further study, such as microbiome analysis, may be needed to elucidate the role of BR polyphenols, which seem to have a potent activity in reduction of cecal TMA level via modulation of gut bacteria.

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