Regular article

日本食品化学学会誌、Vol. 32(2), 52-58 (2025)
Japanese Journal of Food Chemistry and Safety (JJFCS)

Effects of natto-derived fractions on liver metabolic markers and cognitive function in high-fat diet-fed mice

(Received August 30, 2024)
(Accepted January 23, 2025)

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Abstract

Non-alcoholic fatty liver disease (NAFLD) and cognitive decline are global health issues with limited effective pharmacological treatments, making lifestyle modifications, particularly dietary interventions, the most viable option. This study investigated the effects of the 80% ethanol soluble fraction (80ESF) and solid-phase extraction fraction (SEF) from natto, a traditional Japanese fermented soybean product, on high-fat diet (HFD)-induced NAFLD and cognitive decline in mice. HFD significantly increased body and liver weight; however, these increases tended to be suppressed by 80ESF and SEF administration. Furthermore, HFD intake significantly elevated plasma AST, ALT, and LDL cholesterol levels, which were reduced by 80ESF and SEF administration. Additionally, HFD-induced cognitive decline showed improvement trends with 80ESF and SEF. No significant differences were observed between 80ESF and SEF. The findings suggest that natto fractions attenuated HFD-induced liver damage and the associated cognitive decline.

Keywords : cognitive decline, high-fat diet, natto, non-alcoholic fatty liver disease, soybean

Ⅰ Introduction

Non-alcoholic fatty liver disease (NAFLD) is increasingly being recognized as a global health issue, affecting 1.24 billion people worldwide, with cases increasing annually by approximately 1.00%, posing a significant burden on modern society[1)]. Numerous human studies have shown that patients with NAFLD are at a higher risk of developing cognitive impairment. For example, a prospective cohort study demonstrated that NAFLD is a strong risk factor for the development of cognitive impairment in participants aged 45–65[2)]. Another large-scale cohort study involving 4,031,948 subjects aged 40–69 years indicated that NAFLD is associated with an increased risk of dementia[3)]. Numerous animal studies have demonstrated that feeding rodents a high-fat diet (HFD) leads to cognitive impairment through hippocampal neuronal damage, including oxidative stress, neuro-inflammation, and brain insulin resistance[4)]. Therefore, HFD-fed rodent models are widely utilized to study metabolic syndrome and concurrently study cognitive impairment.

As the aging population continues to increase, the severity of NAFLD, cognitive decline, and other diseases caused by unhealthy lifestyles are also expected to rise. Currently, no cure exists for NAFLD or cognitive decline. Therefore, lifestyle modifications, including diet and exercise, remain the primary recommendations for managing NAFLD and the associated cognitive decline[3)].

Dietary interventions have emerged as a promising approach to prevent NAFLD and cognitive decline owing to their low cost and ease of implementation on a broad scale[5, 6)]. Among various dietary components, soybeans stand out for their rich nutritional profile, which includes essential lipids, proteins, carbohydrates, minerals, vitamins, and amino acids[7)]. Compared to raw soybeans, fermented soybean products offer additional benefits through microbial activity, such as enhanced digestibility, reduced anti-nutritional factors, and increased

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