

Effects of *Trigonella foenum-graecum* seeds extract on Alzheimer's disease transgenic model mouse and its potential active compound transferred to the brain

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Abstract

Trigonella foenum-graecum seeds (TF) (Fabaceae) is a well-known plant traditionally used as food and medicinal herb. A variety of pharmacological effects of TF extract were shown against diabetic, cancer and dementia in animal models. Concerning anti-dementia effects of TF extract, it has not been evaluated in Alzheimer's disease models. In addition, those previous studies, active constituents in TF extract for memory function were not identified. We aimed to clarify effects of 30% ethanol TF extract on Alzheimer's disease model, 5XFAD mouse, and determine a major active compound in the brain after oral intake of TF extract. Trigonelline content in TF extract and trigonelline penetration in the brain after oral administration of TF extract (5000 mg/kg, once) were quantified by LC-MS/MS analysis. Memory recovery by TF extract (100, 500 mg/kg/day for 17 days) was evaluated by object location memory test. Expression level of neurofilament light in the cerebral cortex was quantified by western blotting.

Trigonelline was detected in the cerebral cortex of 5XFAD mice 24 h after oral administration of TF extract. Oral administration of TF extract (500 mg/kg/day) for 17 days improved object location memory. TF extract increased dose-dependently the level of axonal protein, neurofilament light in 5XFAD mice. These results suggest that TF extract could be an expected therapeutic candidate for Alzheimer's disease, and supposed one of active compounds transferred in the brain is trigonelline. This study is the first report to determine trigonelline penetration in the brain after oral administration of TF extract.

Keywords : trigonelline, 5XFAD mice, memory recovery, neurofilament light

I Introduction

Trigonella foenum-graecum (Fabaceae), (English name is Fenugreek) is a traditional medicinal plant widely cultivated in Egypt, India and Middle Eastern countries¹⁾. Its leaves and seeds have been used as medicine, spice and vegetable in those countries²⁾. A variety of pharmacological effects of *Trigonella foenum-graecum* seeds extract (TF extract) were shown such as antidiabetic, anticancer and antidementia effects using *in vivo* models³⁾. Concerning antidementia effects of TF extract, aluminum chloride-induced amnesia rats^{4, 5)}, diabetic rats^{6, 7)} and scopolamine-injected⁸⁾ mice were used for evaluation, which are not established as Alzheimer's disease models.

In addition, those previous studies didn't identify active constituents in TF extract for memory function.

TF extract contains various categories of constituents including alkaloids, saponins, flavonoids, phenolic acids and so on³⁾. Especially, trigonelline is the most famous and major constituent in TF extract⁹⁾. We recently reported that oral administration of trigonelline recovered memory function in transgenic Alzheimer's disease model 5XFAD mice¹⁰⁾. In the study, we confirmed that trigonelline penetrated in the brain after oral administration¹⁰⁾. Therefore, we hypothesized and aimed to clarify if trigonelline is a major active compound in TF extract, TF extract administration must improve memory function in 5XFAD mice. If it would be confirmed, we give an