

1 1. *Cordyceps Cicadae* Cultured with Deep ocean Water Performs Neuroprotection against D-galactose-induced Neuroinflammation and Memory Deficits in Rat Model

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1. Introduction

Cordyceps cicada, a medicinal fungus, was proven to contain high concentrations of functional ingredients, such as N6-(2-hydroxyethyl)-adenosine (HEA), with antioxidant and anti-inflammatory effects. Our previous studies found that deep ocean water (DOW) increased the health effect of fungus-fermented product against diseases developments due to the DOW-raised functional compounds and a synergistic effect.

2. Materials and Methods

.This study investigated the effect of a *Cordyceps cicada*-fermented products cultured with DOW (DCC), ultra-pure water (UCC), and a MgCl₂ solution (MgCC) on the prevention of neurodegradation and memory deficit in rats induced by d-galactose injection.

3. Result and Discussion

DCC and its functional component HEA had

the effect of improving memory and learning ability in the rats with memory deficit induced by d-galactose injection. DCC increased glutathione peroxidase (GPx) and superoxidase dismutase (SOD) activities ($p < 0.05$), and further scavenged free radicals and lowered oxidative stress. DCC and MgCC repressed pro-inflammatory factors including tumor necrosis factor alpha (TNF- α), interleukin 6 (IL-6) and interleukin 1 beta (IL-1 β), and further decreased the downstream factors cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). In addition, DCC and MgCC reduced the aging-related proteins glial fibrillary acidic protein (GFAP) and presenilin 1 (PS1) expressions. This study indicated that both DCC and MgCC performed more neuroprotection than UCC through anti-inflammation, antioxidant, and anti-brain aging effects, which suggested that Mg²⁺ may be the functional ion for increasing neuroprotective effects of *C. cicada*.