Acanthopanax senticosus HARMS exerts its anxiolytic effects via regulation of autonomic function and activation of hippocampal brain-derived neurotrophic factor signaling

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[Objective]

There have been several reports of the anxiolytic and anti-stress effects of *Acanthopanax senticosus* HARMS, but few reports studied the mechanism of these effects and the anxiolytic effects of *Acanthopanax senticosus* HARMS were therefore evaluated in detail in this study.

[Methods]

1) Novel environment test

Animals are known to take longer time to begin eating due to anxiety when they are placed in novel environment. Male SD rats were transferred from cages where they were originally housed (home cages) to different cages (novel cages) that were covered with a blackout curtain on the sides and bottom, and their latency to eat in novel cages was measured and autonomic function (activity of sympathetic and parasympathetic nerves) was also measured with a bioelectric potential transmitter attached to rats. *Acanthopanax senticosus* HARMS extracts was mixed with diet and given for 1 week prior to testing.

2) Elevated beam waking test

If rats are placed on the open arm without walls of an elevated beam device (190 cm height x 8 cm width x 140 cm length; closed arm placed at one end [safe room with 3 sides covered with walls]), they immediately move to the safe room due to anxiety or fear. Male SD rats were placed on the open arm of the elevated beam device to measure their time stayed on the open arm and autonomic function until entering the safe closed arm. In addition, the expression levels of hippocampal brain-derived neurotrophic factor (BDNF) and high-affinity BDNF receptor TrkB were measured after the elevated beam waking test. Acanthopanax senticosus HARMS extracts was mixed with diet and given for 1 week prior to testing.

[Results]

1) Novel environment test

In the control group, their time to start eating was markedly prolonged by transferring from their home cages to novel cages, whereas the latency to eat was significantly shortened in the groups given diet containing 1% and 5% *Acanthopanax senticosus* HARMS compared with the control group although it was longer than that when they were kept in home cages

(Figure 1). In the group treated with *Acanthopanax senticosus* HARMS, sympathetic activity was significantly decreased and parasympathetic activity was significantly increased in novel cage compared with the control group (Figure 1).

2) Elevated beam waking test

The time stayed on the open arm was significantly prolonged in the groups treated with *Acanthopanax senticosus* HARMS compared with the control group (Figure 2). In the control group, sympathetic activity was significantly increased and parasympathetic activity was significantly decreased when they were placed on the elevated beam device compared with when they were kept in home cages, whereas these changes were significantly reduced in the groups treated with *Acanthopanax senticosus* HARMS (Figure 3). In addition, the expression levels of hippocampal BDNF and TrkB were increased in the groups treated with *Acanthopanax senticosus* HARMS compared with the control group (Figure 4).

Based on these results, the anxiolytic effects of *Acanthopanax senticosus* HARMS suggested to exert through regulation of autonomic function and activation of hippocampal BDNF signaling.

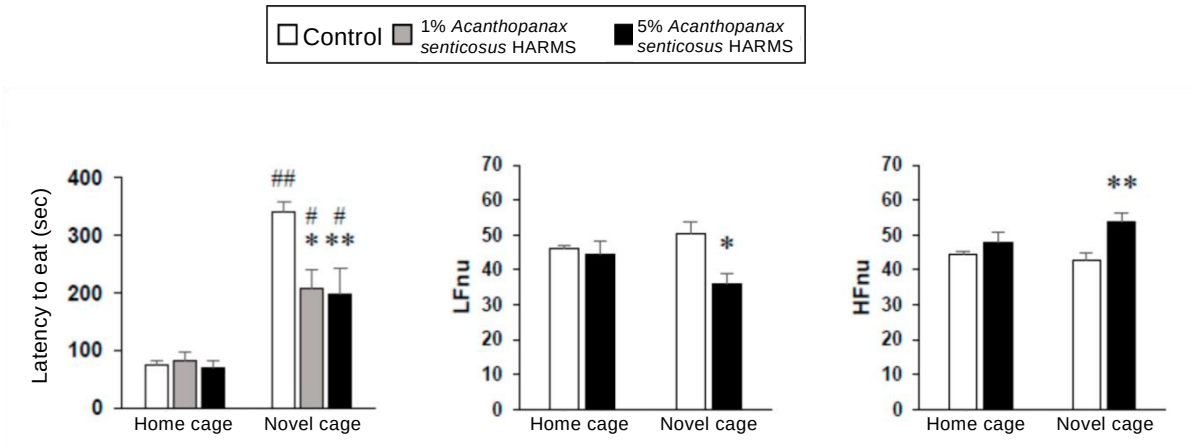

Figure 1. Novel environmental test: Effects on latency to eat and autonomic activity
(#p < 0.05, ##p < 0.01, vs home cage. *p < 0.05, **p < 0.01, vs novel cage/control group, n = 6)

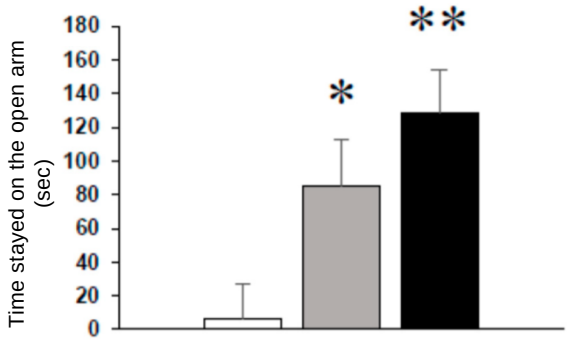

Figure 2. Elevated beam waking test: Effect of *Acanthopanax senticosus* HARMS on the time stayed on the open arm
(*p < 0.05, **p < 0.01, vs control group, n = 8)

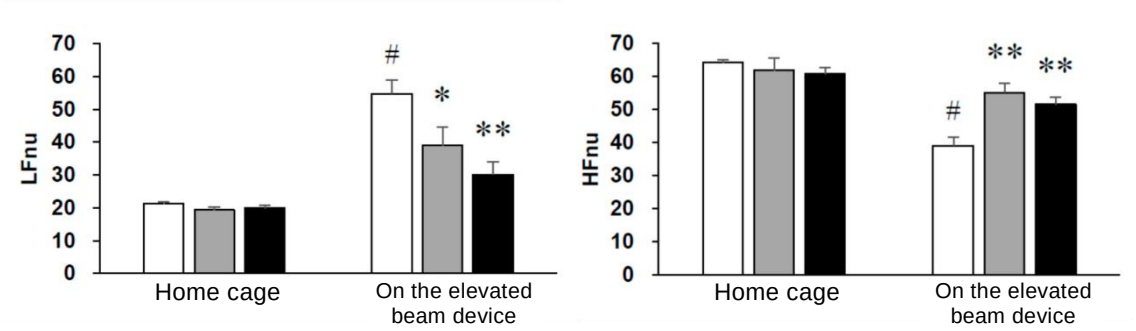

Figure 3. Elevated beam waking test: Effect of *Acanthopanax senticosus* HARMS on autonomic activity

(#p < 0.05, vs home cage.*p < 0.05, **p < 0.01, vs on the elevated beam device/control group, n = 8)

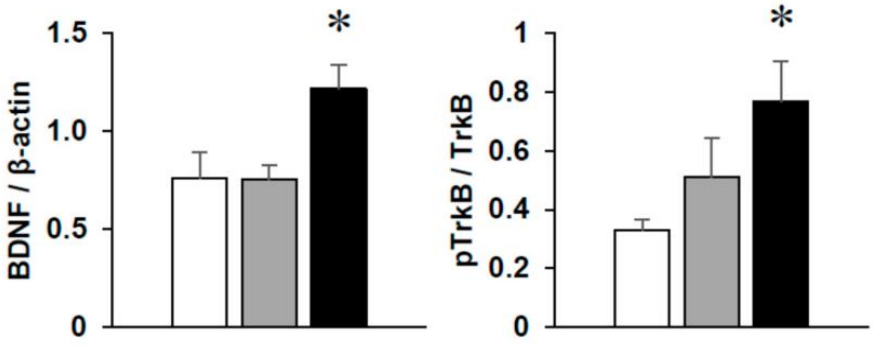

Figure 4. Effects of *Acanthopanax senticosus* HARMS on the expression levels of BDNF and TrkB in the elevated beam waking test

(*p < 0.05 vs control group, n = 4 to 5)

<<Glossary>>

LFnu: A parameter of sympathetic activity determined by frequency analysis of electrocardiogram (ECG). The value increases due to stress such as anxiety and fear.

HFnu: A parameter of parasympathetic activity determined by frequency analysis of ECG. The value decreases due to stress such as anxiety and fear.

BDNF: Brain-derived neurotrophic factor (BDNF); A secretory protein that acts in the development, growth, maintenance, and repair of neurons and also plays important roles in learning, memory, emotion, etc. Recently, it has been confirmed that BDNF is reduced in the brain, mainly hippocampus and cerebral cortex, in patients with depression, Alzheimer's disease, anxiety states, etc.

TrkB: High-affinity BDNF receptor; BDNF exerts various physiological functions through TrkB.

<<Details>>

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