



# Anti-nociceptive effects of *Paecilomyces hepiali* via multiple pathways in mouse models

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**ABSTRACT.** *Paecilomyces hepiali* (PH), a well-known medicinal fungus, has various pharmacological efficacies. In our study, the antinociceptive effects of PH and underlying mechanisms were evaluated using various mouse models. An acetic acid-induced writhing test, hot plate test, and formalin test were employed to evaluate the antinociceptive activities of PH. The levels of neuronal nitric oxide synthase (nNOS) in the hypothalamus and monoamine neurotransmitters in the serum and hypothalamus of experimental mice were examined. Additionally, hot plate tests using mice pretreated with various antagonists were used to determine the mechanisms of PH-mediated antinociception. The PH-enhanced latency period of mice in the hot plate test was significantly blocked by pretreatment with atropine and glibenclamide. PH shortened the phase I and phase II reaction times of formalin-treated mice. Strongly reduced writhing and stretching induced by acetic acid were observed in PH-treated mice,

indicating that PH mainly exerts antinociceptive activity on neurogenic pain. After thermal pain stimulation for 30 s, compared to control mice, 7-day PH-treated mice had lower nNOS and dopamine levels, and increased levels of serotonin in both the serum and hypothalamus. Collectively, our data showed that PH mediated antinociceptive activities via multiple pathways, including monoamines, nNOS/ATP-sensitive K<sup>+</sup> channels, and M-type acetylcholine receptors.

**Key words:** *Paecilomyces hepiali*; Antinociception; Monoamines; nNOS; K<sub>ATP</sub>; mAChR