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RESEARCH REPORTS

Pharmacological modulation of farnesyltransferase subtype I attenuates mecamylamine-precipitated nicotine withdrawal syndrome in mice

Singh, Thakur G.; Rehni, Ashish K.; Arora, Sandeep K.

Author Information
Chitkara College of Pharmacy, Chitkara University, Chandigarh, Punjab, India

Correspondence to Ashish K. Rehni, PhD, Chitkara College of Pharmacy, Chitkara University, Patiala National Highway, Rajpura, Patiala 140401, Punjab, India E-mail: ashishkrehni@gmail.com; gurjeetthakur@gmail.com

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Abstract

This study was designed to investigate the effect of FTI-276 trifluoroacetate, a selective inhibitor of subtype I, on the development of the mecamylamine-induced nicotine withdrawal syndrome. Mice were administered nicotine (2.5 mg/kg, subcutaneously) four times daily for 7 days. To precipitate nicotine withdrawal, mice were administered one injection of mecamylamine (3 mg/kg, intraperitoneally) 1 h after the last nicotine injection on the test day (day 8). Behavioral observations were made for a period of 30 min immediately after mecamylamine treatment. FTI-276 trifluoroacetate treatment markedly and dose-dependently attenuated the precipitated nicotine withdrawal syndrome, measured by a composite withdrawal severity score, jumping frequency, hyperalgesia in the tail flick test, and anxiety-like behavior in the elevated plus maze test. The results suggest that FTI-276 trifluoroacetate can inhibit the development of a precipitated nicotine withdrawal syndrome, and thus that farnesyltransferase subtype I may be a viable pharmacological target to tackle the problem of nicotine addiction.

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