EFFECT OF MENTHOL ON NICOTINE PHARMACOKINETICS IN RATS AFTER CIGARETTE SMOKE INHALATION

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Abstract: The effect of menthol on the absorption and metabolism of nicotine is still unclear. The present study was designed to evaluate, using the rat as an animal model, whether menthol affects the pharmacokinetics of nicotine after either a single-cigarette or multiple cigarette-smoke inhalation. For the single-cigarette smoke inhalation experiment, fasted jugular vein-cannulated rats (n=8) were exposed to mainstream smoke from either a non-mentholated or mentholated cigarette (1 puff/min for 10 min) using a cigarette smoke inhalation apparatus designed to simulate the smoking of a single cigarette. For the multiple-cigarette smoke inhalation experiment, rats (n=8) received the smoke from either one non-mentholated cigarette or one mentholated cigarette (10 puffs) every 12 hours for a total of 17 cigarettes. Serial blood samples were collected during the 10-min inhalation phase for the single-cigarette smoke or the 17th cigarette inhalation, and for 30 hours then after. Nicotine and its major metabolite cotinine were assayed in plasma by radioimmunoassay methods. The nicotine yield and nicotine content values for the non-mentholated cigarette were similar to those for the mentholated cigarette. Following single-cigarette smoke inhalation, mentholated cigarettes significantly decreased the mean peak concentrations of nicotine in plasma (Cmax) from 27.1 to 9.61 ng/ml, and the total area under the plasma concentration-time curves (AUC) from 977 to 391 ng-min/ml as compared to those after non-mentholated cigarette smoke inhalation. Cmax and AUC values for cotinine were also significantly reduced by menthol. Similarly, Cmax, AUC, and the mean average steady-state plasma concentration of nicotine as well as cotinine were significantly low in multiple-mentholated cigarette inhalation rats as compared to the multiple non-mentholated cigarette inhalation rats. Interestingly, there was a significant increase in the cotinine to nicotine AUC ratio from 14.6 for the non-mentholated cigarette to 21.2 for the mentholated cigarette. These results suggest that menthol in mentholated cigarettes can substantially decrease the absorption and/or increase the clearance of nicotine.

Key words: Menthol, pharmacokinetics, nicotine, smoking

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