Review

Cytisine for the treatment of nicotine addiction: from a molecule to therapeutic efficacy

Piotr Tutka¹, Witold Zatoński²

¹Department of Experimental and Clinical Pharmacology, Medical University of Lublin, Jacekowskiego 8, PL 20-600 Lublin, Poland
²Department of Epidemiology and Cancer Prevention, The M. Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Roentgena 4, PL 02-781 Warszawa, Poland

Correspondence: Piotr Tutka, e-mail: tutka@am.lublin.pl

Abstract:
Cytisine, a natural plant alkaloid, has been marketed in Central and Eastern Europe for over 40 years for the clinical management of smoking cessation. Despite the fact that cytisine has been used by millions of smokers, its characteristics have not been reviewed in scientific literature in English, and presently existing clinical studies on its effectiveness and safety are insufficient to warrant licensing by modern standards. Understanding of the mechanism of cytisine action as a smoking cessation aid provides a necessary basis for conducting clinical trials to confirm its efficacy as an optimal antismoking therapy. Hereafter, we present a review of current knowledge about the pharmacokinetics, pharmacodynamics, toxicity, therapeutic efficacy and safety of cytisine, and about its derivatives that are under development. Recent pharmacological research has elucidated that the drug is a low efficacy partial agonist of α4β2 nicotinic acetylcholine receptors, which are believed to be central to the effect of nicotine (NIC) on the reward pathway. The drug reduces the effects of NIC on dopamine release in the mesolimbic system when given alone, while simultaneously attenuating NIC withdrawal symptoms that accompany cessation attempts. Clinical studies on cytisine as a smoking cessation aid have demonstrated that the drug is effective and safe. Our recent uncontrolled trial has shown that a 12-month carbon monoxide-verified continuous abstinence rate following a standard course of treatment with cytisine with minimal behavioral support is similar (13.8%; N = 436) to that observed following treatment with NIC replacement therapy. Since cytisine exhibits a desirable pharmacological profile which makes it an attractive smoking cessation drug, it should be advanced to randomized clinical trials. However, more detailed preclinical studies on its pharmacokinetics and safety profile are required.

Key words:
cytisine, nicotine addiction, smoking cessation, nicotine, dopamine, tobacco dependence, varenicline