Pharmacokinetics and metabolism of nicotine

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Abstract:
Nicotine (NIC), the major constituent of tobacco, is responsible for the compulsive use of tobacco. Advances in understanding of the pharmacokinetics and metabolism of NIC have been made rapidly over the past decade. The application of highly sensitive gas chromatography/mass spectrometry led to the identification and quantitation of new NIC metabolites as well as characterization of new pathways of NIC biotransformation. This review summarizes findings from human and animal studies concerning NIC kinetics and biotransformation as well as describes the factors that influence these processes.

Recently, large individual, racial and species differences in the metabolism of NIC have been well documented. The differences in the metabolism of NIC may be a result of genetic, environmental, and developmental host influences. We review the scientific evidence from studies that supports a role for genetic mechanisms responsible for variability in the profile and the rate of the NIC metabolism. Actually, the majority of the genetic studies focus on the characterization of the CYP2A6 gene polymorphism, and on determining the relationship between the phenotype of NIC metabolism and the genotype of the CYP2A6 gene. There is good evidence that genetic polymorphisms associated with NIC metabolism are an important factor responsible for susceptibility to NIC dependence. It is anticipated that genetic findings can lead to the identification of individuals at a greater risk for tobacco addiction and will be used for more effective treatment and prevention strategies to reduce smoking.

Key words:
nicotine, cotinine, tobacco, smoking, nicotine metabolism, CYP2A6