

A Review of the Evidence on Impairment of Antihistamines and Driving Ability

The driving risks due to alcohol use are well known and in 2002, there were 17,970 alcohol-related crashes in the United States. There has also been a growing awareness of the traffic safety risks due to the behavioral toxicity of drugs other than alcohol. These include not only illicit drugs, such as cocaine and marijuana, but also medicinal drugs that are available over-the-counter or by prescription.

Widespread use of antihistamines (histamine H₁-receptor antagonists, or H₁-antagonists) present a particular concern since the first-generation antihistamines are well known for causing sedation and central nervous system (CNS) dysfunction that can jeopardize safe driving. Antihistamines also have additive effects with alcohol and other CNS depressants. These drugs are widely used and are available in both over-the-counter and prescription treatments for colds, allergies, and hay fever. Second-generation antihistamines have been produced in the last decade. These are associated with fewer side effects and have fewer reports of sedation. Currently, there are more than 60 oral antihistamines available.

The National Highway Traffic Safety Administration sponsored a review of the evidence on impairment of antihistamines on driving ability by the Southern California Research Institute. The institute reviewed the scientific literature from several perspectives: epidemiological studies, laboratory tests of driving related skills, and simulator and on-the-road studies. The five most widely prescribed or studied drugs from each generation of antihistamines were included. There are six generally recognized chemical classes of antihistamines: alkylamines, ethanoloamines, piperazines, ethylenediamines, phenothiazines, and piperidines.

Antihistamines Reviewed

First-generation H₁-receptor antagonists		
<i>Generic Name</i>	<i>Trade Name</i>	<i>Drug Class</i>
chlorpheniramine	Chlor-Trimeton	Alkylamines
clemastine	Tavist	Ethanolamine
diphenhydramine	Benadryl	Ethanolamine
hydroxyzine	Atarax	Piperazines
tripolidine	Actidil	Alkylamines
Second-generation H₁-receptor antagonists		
<i>Generic Name</i>	<i>Trade Name</i>	<i>Drug Class</i>
astemizole	Hismanal	Piperidine
certirizine	Zyrtec	Piperidine

fexofenadine	Allegra	Piperidine
loratadine	Claritin	Piperidine
terfenadine	Seldane	Piperidine

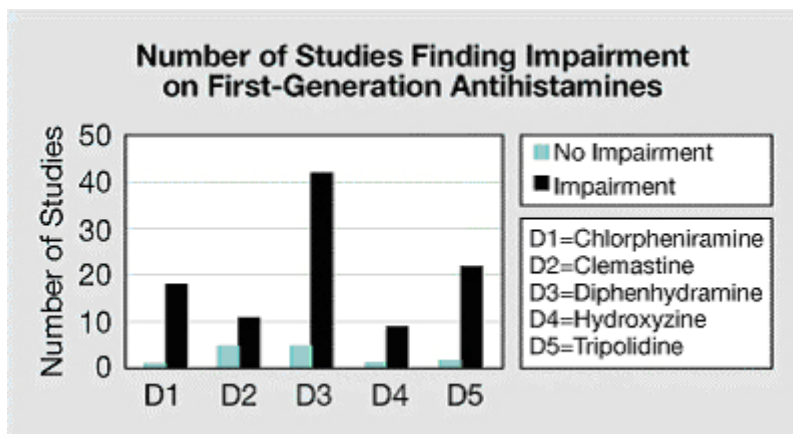
Performance measures were categorized into 10 behavioral categories and one subjective category for both acute and repeated dosing schedules.

- Driving and Piloting
- Psychomotor
- Perception
- Visual Functions
- Cognitive Tasks
- Divided Attention
- Vigilance
- Tracking
- Reaction Time
- Physiological
- Subjective Sedation

Findings

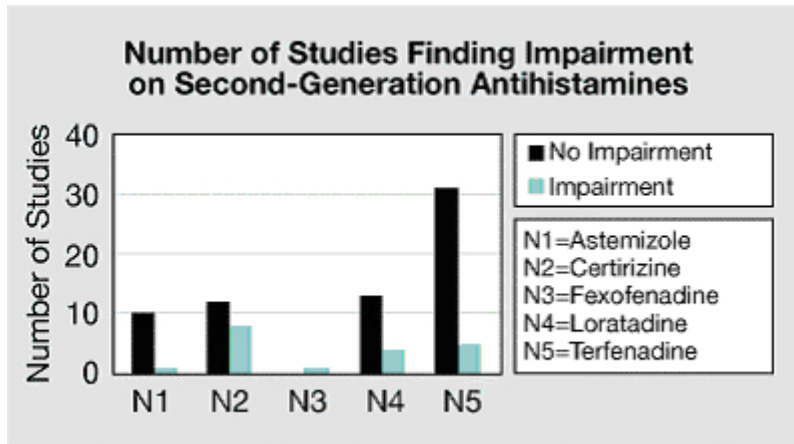
There is some slight, but ambiguous, evidence from epidemiological studies of a connection between antihistamine use and traffic crash rates. These epidemiological studies were done primarily when the use of first-generation (but no second-generation) antihistamines was prevalent.

There is overwhelming evidence from the experimental literature that the first-generation antihistamines produce objective signs of skills performance impairment as well as subjective symptoms of sedation.



In contrast, second-generation antihistamines show much fewer incidence of objective skills performance impairment and, in the majority of cases, no evidence of subjective sedation.

While second-generation antihistamines represent a major triumph for the pharmaceutical industry in reducing potential side effects, there still remains some evidence that all antihistamines have objective skills impairment consequences.



Within both groupings of antihistamines, there is considerable variation in objective evidence of impairment. For the first-generation antihistamines, there is variation in subjective effects (such as sedation). Within each generation, there clearly are preferred drugs used to avoid side effects.

The researchers note that the rate of impairment can be manipulated by studies that fail to use sensitive performance measures or to test at appropriate post-dose times. Some methods are more sensitive than others.

For drivers seeking treatment for the symptoms of colds, flu, and allergies, the proper selection of second-generation antihistamines should produce little impairment of skilled performance, such as driving.

How To Order

For a copy of *Antihistamine and Driving-Related Behavior: A Review of the Evidence for Impairment for First- versus Second-Generation H₁-Antagonists* (32 pages plus extensive appendices), write to the Office of Research and Technology, NHTSA, NTI-130, 400 Seventh Street, SW., Washington, DC 20590 or fax 202-366-7096, or download from www.nhtsa.dot.gov. Richard Compton, Ph.D., was the contract manager.

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